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PRECANCEROUS DERMATOSIS AND EPITHELIOMA IN SITU

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The term "precancerous dermatosis" (precancerosis of Bloch [1]) is based on clinical, statistical and histopathologic concepts. The term has been used loosely by many authors [2] to include many cutaneous diseases in which the incidence of carcinoma is no greater than should be expected when the varying factors of age, senile cutaneous changes, exposure and sensitivity to light, chronic and persistent irritation or trauma and the effects of previous therapy, all of which may predispose to carcinoma, are considered. As a working basis I wish to limit the term "precancerous dermatosis" to true but infrequent Bowen's [3] precancerous dermatosis, senile keratosis, keratosis resulting from arsenic, tar or radiation and various forms of leukoplakia of the mucous membrane of the mouth and genitalia, including so-called erythroplasia of Queyrat. I shall show that in 20 per cent or more of cases of all these conditions epithelioma develops, usually of squamous cell type and, beginning in situ, associated with various phenomena of dyskeratosis and keratinization of individual cells simulating most closely the histologic picture of Bowen's disease.

On the basis of most specimens submitted to pathologists the diagnosis of carcinoma or a benign process can readily be made. However, when lesions about the benign or malignant character of which there is

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1. Bloch, B.: Cancers and Precancerous Affections from the Dermatological Viewpoint, Cancer Rev. **7**:65-98 (Feb.) 1932.

2. (*a*) Eller, J. J.: The Role of Physical Therapy in the Treatment of Precancerous and Cancerous Dermatoses, J. A. M. A. **100**:385-388 (Feb. 11) 1933. (*b*) Eller, J. J., and Anderson, N. P.: Cancer Supervention in Skin Diseases: Clinical, Microscopic and Therapeutic Considerations, ibid. **94**:382-385 (Feb. 8) 1930. (*c*) Goldman, L.: Precancerous Lesions of the Skin, J. Med. **17**:278-285 (Aug.) 1936. (*d*) MacKee, G. M., and Cipollaro, A. C.: Cutaneous Cancer and Precancer: A Practical Monograph, New York, American Journal of Cancer Publishing Company, 1937, p. 46. (*e*) Missildine, J. G., and Van Cleve, J. V.: Precancerous Dermatoses, J. Kansas M. Soc. **37**:187-190 (May) 1936.

3. Bowen, J. T.: Precancerous Dermatoses: A Study of Two Cases of Chronic Atypical Epithelial Proliferation, J. Cutan. Dis. **30**:241-255 (May) 1912.

doubt clinically are selected critically for biopsy, the same doubt often exists pathologically. Thus, distinction between benign and malignant dyskeratosis and what might be accepted as early squamous cell epithelioma in situ may be difficult. Conversely, many lesions of precancerous dermatoses may remain as such without increase in size over a period of twenty or more years, and yet the histologic picture is definitely that of squamous cell epithelioma in situ.

Xeroderma pigmentosum might also be included with the precancerous dermatoses but for the factors of heredity and sensitivity to light of certain wavelengths that predispose to malignant change [4] and the histologic picture, which is usually that of basal cell epithelioma. In the absence of exposure to actinic rays, malignant change may not occur.

This study is based on fifteen years' experience in correlating the clinical and histologic changes observed in cases of precancerous dermatosis together with a critical review of the voluminous literature on this subject, of which only a few of the more pertinent or more recent articles will be cited.

DYSKERATOSIS AND MALIGNANT CHANGE

Darier used the term "dyskeratosis" originally to include benign conditions such as molluscum contagiosum and Darier's disease, as well as Bowen's disease and Paget's disease of the nipple. He [5] recently gave the following definition of this term:

> Je dirai incidemment que ce nom (cellules dyskératoseques), qui a été critiqué, ne signifiait pas dans mon esprit qu'elles sont kératinisées, mais seulement qu'elles ont subi une modification de leur évolution normal, devant les conduire à la kératinisation; le terme de cellules "en dyskératinisation" serait donc si l'on veut plus exact.

Kogoj [6] and Pautrier [7] used the term dyskeratosis in a more limited sense as applied especially to the round bodies (*corps ronds*) and still more keratinized cells known as grains, which are seen especially in Darier's disease but may be seen in many cutaneous diseases, especially granuloma, and are therefore without diagnostic significance. Darier's definition of dyskeratosis admits any modification in the normal evolution of the cells of the epidermis, namely, any abnormal phenomenon

4. Lynch, F. W.: Xeroderma Pigmentosum: Study in Sensitivity to Light, Arch. Dermat. & Syph. **29**:858-873 (June) 1934. Montgomery, H., and Reuter, M. J.: Xeroderma Pigmentosum: Report of a Mild Case with Histopathologic Studies, ibid. **26**:256-267 (Aug.) 1932.

5. Darier, M.: Maladie de Paget à son début: Epithélioma canaliculaire sous-jacent, Bull. Soc. franç. de dermat. et syph. **34**:156-157 (March 10) 1927.

6. Kogoj, F.: La dyskératose, Ann. de dermat. et syph. **8**:351-373 (June) 1927.

7. Pautrier, L. M.: "Paget's Disease of the Nipple": A True Cancer Tending to Invade the Epidermis and Necessitating Total and Early Amputation of the Breast, Arch. Dermat. & Syph. **17**:767-790 (June) 1928.

of keratinization. Broders [8] and I [9] have used the term "individual cell keratinization" to express the phenomenon of malignant dyskeratosis of individual cells of the epidermis, as seen most clearly in cases of Bowen's disease. Thus, disorganization of the normal arrangement and size of the cells of the epidermis and amitosis as well as mitosis resulting in the formation of epithelial giant cells and giant epithelial cells may be regarded as a malignant type of dyskeratosis. Satenstein [10] used the terms "accelerated" and "retarded" for types of keratinization, to distinguish between benign and malignant dyskeratosis. Neither Charache's [11] nor Wende's [12] cases can be accepted, I believe, as evidence of malignant change in lesions of Darier's disease. *Corps ronds* and grains, however, may be seen side by side with cells which morphologically are malignant and show evidence of individual keratinization.

BOWEN'S DISEASE

The term "Bowen's disease" has been used loosely in the literature to include many conditions, especially those in which lesions occur on the mucous membranes and in which, clinically as well as pathologically, the picture is that of superficial moist squamous cell epithelioma in situ or even of ordinary invading squamous cell epithelioma. I should limit the use of the term "Bowen's disease" to those lesions resembling Bowen's original description, simulating noduloulcerative syphiloderm, and possibly to the type of multiple lenticular plaques described by Darier and by Fraser.[13] I have had the opportunity of studying a total of 10 cases of Bowen's disease, 6 of them at the clinic. In all but 1 of these cases there was a solitary plaque, and in all the disease was limited to the glabrous skin. The shortest duration at the time of examination was six years (fig. 1*a*) and the longest, thirty years, without a clinical history of any progression in size of the lesions. In none of the 6 cases was there any history of ingestion of arsenic or evidence of arsenical pigmentation, arsenical keratosis or superficial epitheliomatosis. In none of the cases was there any history of recurrence from two to eleven years after treatment. The following 3 cases are cited as illustrative of true Bowen's disease.

8. Broders, A. C.: Carcinoma in Situ Contrasted with Benign Penetrating Epithelium, J. A. M. A. **99**:1670-1674 (Nov. 12) 1932.

9. Montgomery, H.: Superficial Epitheliomatosis, Arch. Dermat. & Syph. **20**:339-357 (Sept.) 1929.

10. Satenstein, D. L.: Histologic Evidence of Epithelioma of the Skin, Arch. Dermat. & Syph. **33**:48-59 (Jan.) 1936.

11. Charache, H.: Darier's Disease with Malignant Transformation, Arch. Dermat. & Syph. **35**:480-484 (March) 1937.

12. Wende, G. W., cited by Charache.[11]

13. Fraser, J. F.: Bowen's Disease and Paget's Disease of the Nipple: Their Relation to Dyskeratosis, Arch. Dermat. & Syph. **18**:809-828 (Dec.) 1928.

REPORT OF CASES

CASE 1.—A woman aged 54 was seen at the Mayo Clinic in July 1926, because of a plaque on the right upper portion of the abdomen of eighteen years' duration. The lesion had started as a scaling plaque. At times there had been crusting and slight bleeding or serous discharge whenever the clothing caught on the scales or crusts. The lesion had shown a tendency to heal at times. Examination showed

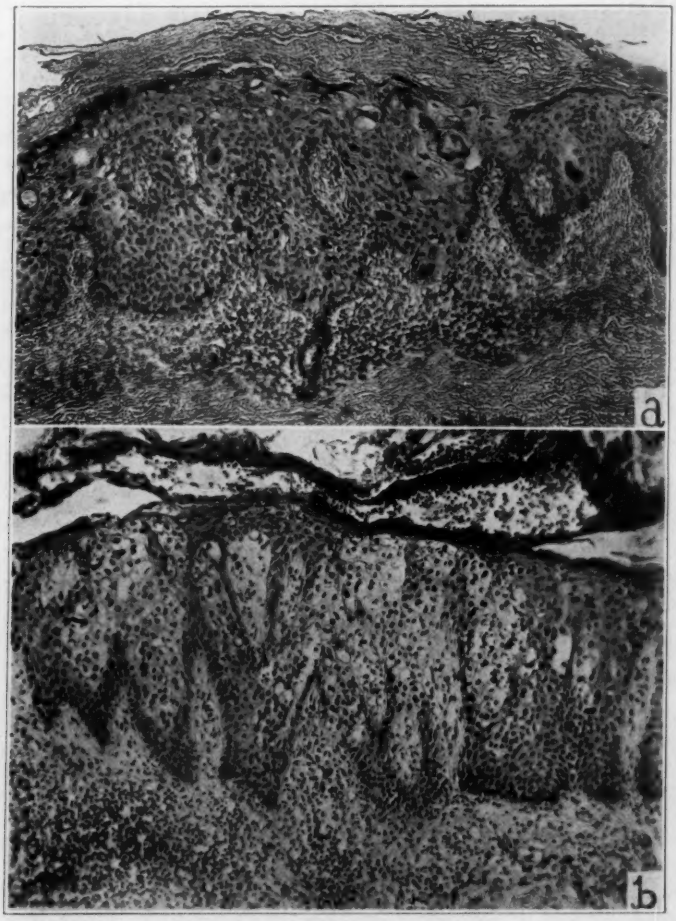

Fig. 1.—Bowen's disease: *a*, typical-appearing squamous cell epithelioma of grade 1 in situ; amitotic and mitotic division of cells and keratinization of individual cells resulting in epithelial giant cells and giant epithelial cells (× 110); *b*, peculiar vacuolation of cells simulating Paget cells, but with preservation of intercellular bridges, little clumping of cells and few mitotic figures (× 100).

a slightly indurated plaque 3 cm. in diameter, with sharply defined but not pearly borders. There were several nodules and crusts and scales, the removal of which resulted in weeping and bleeding. The clinical appearance of the lesion was atypical for ordinary superficial epitheliomatosis. The histologic picture is shown in figure 1 *b*. There were considerable vacuolation of the cells and relatively few

mitotic figures. Only occasional clumping of the cells to form epithelial giant cells was seen. I felt the picture was classified best as Bowen's disease, and Fraser, to whom sections were sent, concurred in this diagnosis. Broders at first classified the histologic changes as merely inflammatory, but he later concurred in my diagnosis. The vacuolation in this case suggested extramammary Paget's disease, but study under high power magnification revealed preservation of the intracellular bridges and the presence of pyknotic rather than well formed nuclei; the structure of the individual cells was not that of the Paget cell. Contrary to the usual experience with squamous cell epithelioma in situ, the lesion responded to treatment with radium; one new lesion appeared in 1928 and responded to radiotherapy administered elsewhere.

Case 2.—A laborer aged 74 was seen at the clinic in March 1929, because of two superficial crusted infiltrated plaques on the left thigh, which gave evidence of peripheral extension with central healing. The lesions had developed following injury to the leg in 1909. The lesions were excised; this was followed by radiotherapy, including treatment of a few small soft freely movable nodes in the groin. The patient reported no recurrence of the lesions five years later. The histologic picture is shown in figure 2 *a*, and figure 2 *b* represents an enlargement of an area in figure 2 *a*. The microscopic diagnosis was squamous cell epithelioma, grade 2 (on the basis of 1 to 4), occurring chiefly in situ. All the phenomena of Bowen's disease and of keratinization of individual cells are readily seen.

Case 3.—A physician aged 56 had a scaling plaque about 2 cm. in diameter on the leg, of fifteen years' duration. There was a definite arciform configuration of the border, and there were some regions of slight crusting. A history of arsenical medication could not be obtained, and arsenic was not present in the urine. The histologic picture was one of early squamous cell epithelioma in situ, grade 1, with various phenomena of keratinization of individual cells (fig. 3).

Comment.—Figures 1 to 3 illustrate the varying degrees of keratinization of individual cells in the 3 reported cases of Bowen's disease. Many pathologists undoubtedly will regard the lesion in case 1 (fig. 1 *b*) as a benign process, and some may feel the same in regard to that in case 3 (fig. 3). There can be no question as to the pathologic diagnosis of squamous cell epithelioma beginning in situ in regard to figure 1 *a* and figure 2 (case 2). The long duration of the disease in the instances just cited indicates the relative benignity of the process from the clinical aspect. Nevertheless, Bowen's disease may result in invasive squamous cell epithelioma with metastasis and death.

Grütz [14] and Gutmann [15] wrote of Bowen's disease changing into basal cell epithelioma, as did Goldberg.[16] Szodoray [17] wrote of a case

14. Grütz, O.: Klinisch-histologische Beobachtungen zum Problem der Krebsentstehung (Beiträge zur Histologie der Bowenschen präcancerösen Dermatose), Ztschr. f. Krebsforsch. **21**:415-431 (Oct.) 1924.

15. Gutmann, C.: Ueber die Bowensche Dermatose, Dermat. Wchnschr. **80**: 641-645 (May 2) 1925.

16. Goldberg, L. C.: Bowen's Precancerosis with Carcinoma: Report of a Case of Organized Syphilitic Vulvar Papules, Leukoplakia, Bowen's Precancerosis and Basal Cell Carcinoma, Arch. Dermat. & Syph. **36**:47-52 (July) 1937.

17. Szodoray, L.: Histologic Characteristics of the So-Called Precancerous Processes of the Skin, Arch. Dermat. & Syph. **36**:552-560 (Sept.) 1937.

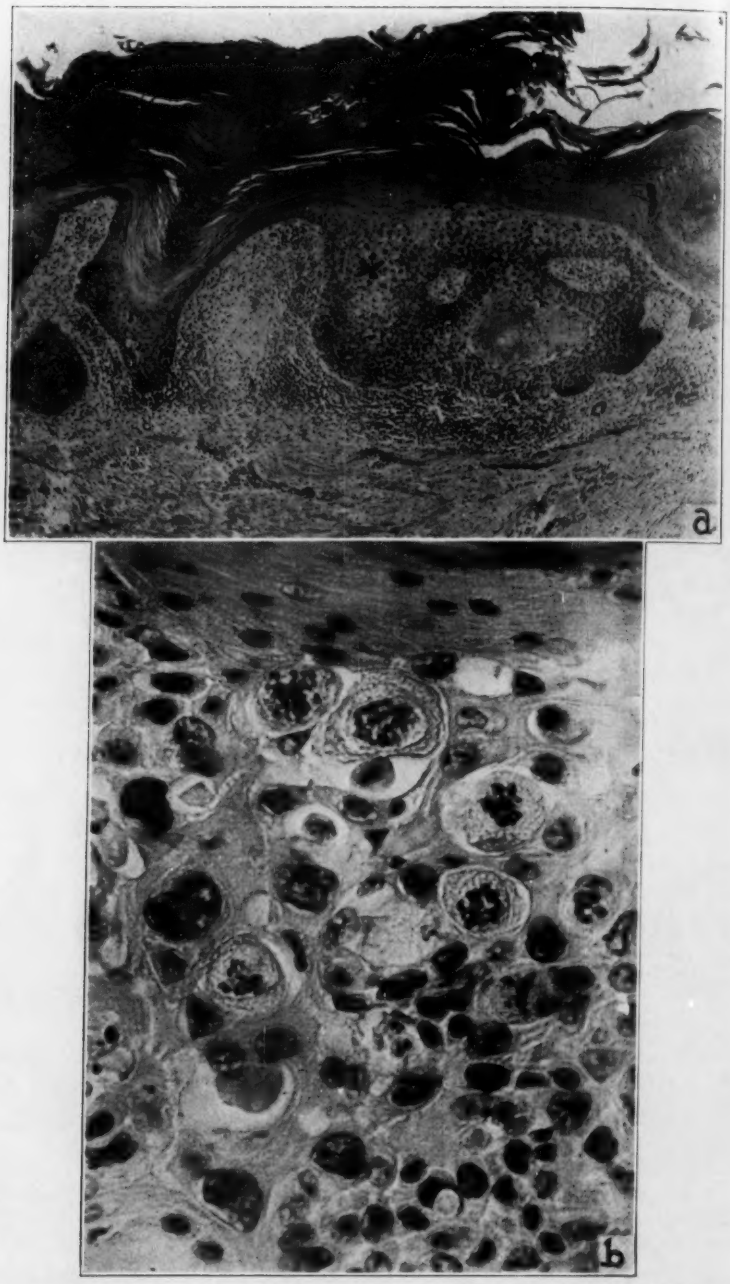

Fig. 2.—Bowen's disease: *a*, squamous cell epithelioma of grade 2 chiefly, in situ, showing extensive hyperkeratosis, various phenomena of malignant dyskeratosis and keratinization of individual cells and usual inflammatory reaction in the upper portions of the cutis; *b*, higher magnification of the area at *X* in *a*, showing amitotic and mitotic division of cells, *corps ronds* and grains (× 435).

of Bowen's disease involving the labia minora, with heterotopic proliferation of basal cells in the central parts of the lesion, and he stated that the growth proceeds from the edges centrally. The photographs accompanying these articles, however, strongly suggested that what is regarded as basal cell epithelioma is actually an undifferentiated squamous cell epithelioma of grade 3 or 4. None of the authors mentioned this possibility. Broders and I have emphasized repeatedly the

Fig. 3.—Bowen's disease: squamous cell epithelioma of grade 1 in situ, with early changes, showing variation in the size of the mitotic figures and in the degree of cells of individual keratinization.

ability of undifferentiated squamous cell epithelioma of grade 4 to simulate the histologic picture of basal cell epithelioma.[18] I do not believe that Bowen's disease ever eventuates in basal cell epithelioma. From the beginning, pathologically, it is squamous cell epithelioma.

18. (*a*) Montgomery, H.: Basal Squamous Cell Epithelioma, Arch. Dermat. & Syph. **18**:50-73 (July) 1928; (*b*) Histogenesis of Basal-Cell Epithelioma, Radiology **25**:8-23 (July) 1935. (*c*) Broders.[8]

The histologic picture of Bowen's disease is not diagnostic but is common to all true precancerous dermatoses. Savatard [19] in a paper headed by the ambiguous term "psoriasiform carcinoma" stated that extramammary Paget's disease and Bowen's disease are variants of superficial epitheliomatosis. Rosenberg [20] supported Savatard's views and even confused the clinical picture of verruca senilis and superficial epitheliomatosis. In most cases, however, Bowen's disease occurs independently of any lesions of superficial epitheliomatosis. Most of the lesions of superficial epitheliomatosis are either of basal cell character or of a moist type which may be basal-squamous or squamous cell epithelioma, and only occasionally show evidence of squamous cell epithelioma in situ with the phenomenon of keratinization of individual cells.

As my associates and I have stated previously,[21] I believe that in most cases so-called extramammary Paget's disease is simply a variant of Bowen's disease or represents superficial moist squamous cell epithelioma or metastatic carcinoma. The Paget cell is distinctive.[22] Because Paget's disease of the nipple is associated with underlying adenocarcinoma of the breast in at least 75 per cent of cases, it should not be included with the precancerous dermatoses. Weiner [23] recently has reviewed cases of true extramammary Paget's disease and has presented a case in which there was a lesion on the labia which, he thought, originated from the apocrine glands. He failed, however, to demonstrate any transition from normal apocrine glands to Paget cells.

Bowen's disease has been assumed to originate from the sebaceous [24] or sweat [25] glands without any definite demonstration by serial section or wax reconstruction that there was a true connection with these struc-

19. Savatard, L.: Psoriasiform Carcinoma of the Skin, Brit. J. Dermat. **47**: 51-64 (Feb.) 1935.

20. Rosenberg, W. A.: Superficial Epitheliomatosis, Arch. Dermat. & Syph. **34**:973-979 (Dec.) 1936.

21. (*a*) Montgomery, H.: Early Recognition and Treatment of Skin Cancer, S. Clin. North America **17**:1249-1264 (Aug.) 1937. (*b*) Montgomery, H.; Counseller, V. S., and Craig, W. McK.: Kraurosis, Leukoplakia and Pruritus Vulvae: Correlation of Clinical and Pathologic Observations with Further Studies Regarding Resection of the Sensory Nerves of the Perineum, Arch. Dermat. & Syph. **30**: 80-100 (July) 1934. Montgomery.[9]

22. Rubenstein, M. W.: Paget's Disease of the Male Nipple and Areola, Arch. Dermat. & Syph. **22**:281-300 (Aug.) 1930. Pautrier.[7] Montgomery.[9]

23. Weiner, H. A.: Paget's Disease of the Skin and Its Relation to Carcinoma of the Apocrine Sweat Glands, Am. J. Cancer **31**:373-403 (Nov.) 1937.

24. Rousset, J.: Les dyskératinisations épithéliomateuses, Paris, Masson & Cie. 1931.

25. Grzybowski, M.: L'évolution du cancer de la maladie de Bowen, Ann. de dermat. et syph. **4**:198-219 (March) 1933; A propos du travail de Jorno "Clinique et histopathogénie de la maladie de Bowen," ibid. **7**:598 (June) 1936.

tures. Multiple sections made in the cases of Bowen's disease observed at the clinic and in other cases of precancerous dermatosis with squamous cell epithelioma in situ have failed uniformly to show involvement of the sweat glands or sebaceous glands. Jorno [26] in a recent review expressed agreement with Darier that Bowen's disease can be regarded as a dyskeratosis in the broad sense of the term. He did not recognize that it originates from a sweat gland or sebaceous gland and pointed out that the sweat glands are unaltered at their orifices. True carcinoma originating from the sweat glands or sebaceous glands is a distinct rarity.[27] Some authors have expressed the belief that Bowen's disease represents a delayed nevus.[14]

Bowen's disease was first described by Bowen,[3] correctly, I believe, as a precancerous dermatosis, and Darier [28] recognized this in subsequently reporting a case under the title "The Cancer of the Precancerous Dermatosis of Bowen." As the term is used generally in the literature today, however, Bowen's disease, or Bowen's epithelioma, has come to mean squamous cell epithelioma which histologically gives evidence of malignant dyskeratosis and the phenomenon of keratinization of individual cells.

SENILE KERATOSIS

What has just been said in regard to the cytologic fundamentals of Bowen's disease is equally applicable to those of senile keratosis. Hookey,[29] working under my supervision, and later Dörffel and I [30] showed that in 20 to 25 per cent of cases of senile keratosis one or more lesions will show evidence of squamous cells epithelioma in situ or invading squamous cell epithelioma with individual cell keratinization, graded 1 to 3 on Broders' basis of classification. The histologic picture may duplicate that of Bowen's disease. Again, all clinical transitions between benign and malignant dyskeratosis are to be seen. Figure 4 *a*, a section of a lesion which appeared clinically to be senile keratosis of the fore-

26. Jorno, M. J.: A propos de la clinique et de l'histopathogénie de la maladie de Bowen, Ann. de dermat. et syph. **7**:369-389 (April) 1936.

27. Flarer, F.: Considérations histogénétiques et cliniques sur les épitheliomes cutanés de dérivation glandulaire sudoripare, Ann. de dermat. et syph. **6**:1073-1106 (Dec.) 1935. Loos, H. O.: Die Carcinome der Anhangsgebilde der Haut, Arch. f. Dermat. u. Syph. **174**:465-510 (Sept. 10) 1936.

28. Darier, J.: Le cancer de la dermatose précancéreuse de Bowen, Ann. de dermat. et syph. **1**:49-61, 1920.

29. Hookey, J. A.: Keratoma Senilis and Verruca Senilis: A Clinical and Histopathologic Study, Arch. Dermat. & Syph. **23**:946-959 (May) 1931; abstracted, Proc. Staff Meet., Mayo Clin. **5**:239-241 (Aug. 27) 1930.

30. (*a*) Montgomery, H.: Verruca Senilis and Keratoma Senile, Minnesota Med. **18**:735-738 (Nov.) 1935. (*b*) Montgomery, H., and Dörffel, J.: Verruca senilis und Keratoma senile, Arch. f. Dermat. u. Syph. **166**:286-296 (Sept. 22) 1932.

head of fifteen years' duration histologically gives evidence of a benign type of dyskeratosis and imitates the histologic picture of Darier's disease. Lacunas, or spaces, in the epidermis, with partially keratinized cells known as *corps ronds* and grains, could be seen lying free in these

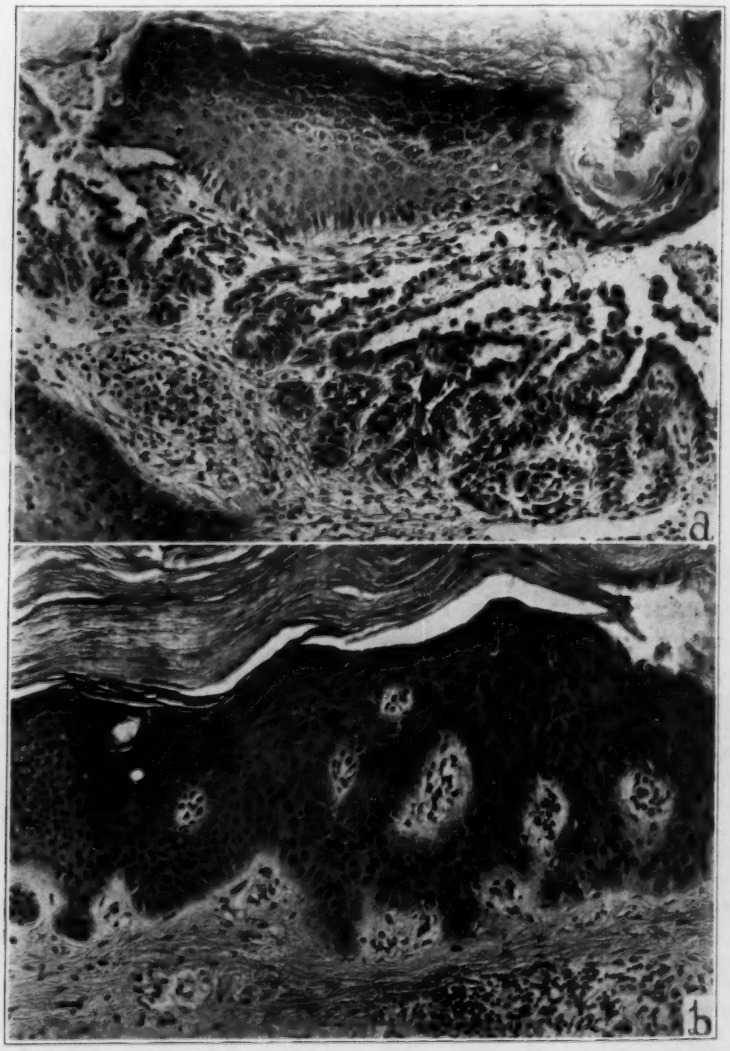

Fig. 4.—Senile keratosis: *a*, section showing lacunas, or spaces, within the epidermis containing *corps ronds* and grains and simulating Darier's disease (× 125); *b*, section showing normal epidermis at the left and changed size and arrangement of prickle cells at the right, without definite malignant changes. The lesion is early squamous cell epithelioma, grade 1, in situ (× 115).

spaces. Figure 4 *b* is a photomicrograph of a section from a typical lesion of senile keratosis on the dorsum of the hand of a man aged 58;

there was a rather abrupt change from relatively normal epidermis to early squamous cell epithelioma of grade 1 in situ. The prickle cells no longer had an orderly arrangement and stained less intensely with hematoxylin than normally. There were many abnormally large cells, with increase in size of the nucleus in proportion to the amount of cytoplasm, a feature indicative of a malignant cell.[31] However, as yet amitosis or mitosis or clumping of cells to form epithelial giant cells could not be demonstrated.

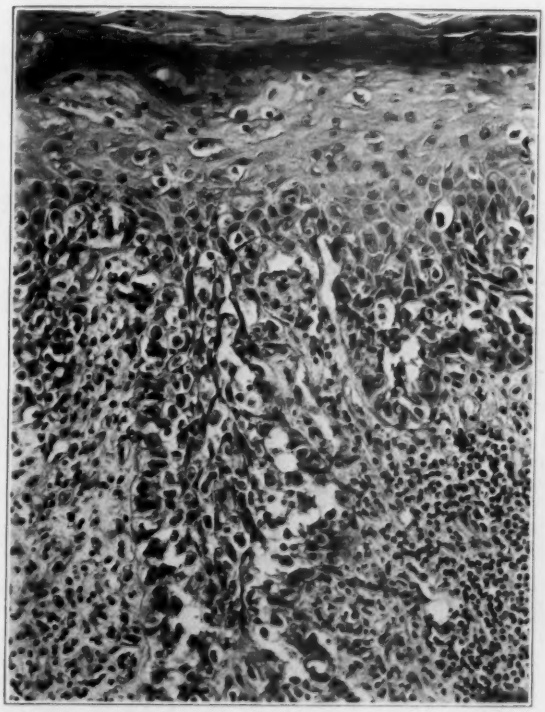

Fig. 5.—Squamous cell epithelioma of grade 2, arising from senile keratosis and simulating Paget's disease; there is extensive dyskeratosis, with numerous mitoses; the intercellular bridges are preserved (× 135).

This type of lesion would not be accepted by many pathologists, I believe, as squamous cell epithelioma. Yet all gradations from this picture to that of invasive squamous cell epithelioma may be seen in sections from the same lesion in many cases of senile keratosis. Figure 5 is a photomicrograph of a lesion obtained from a man aged 66 who had an extensive superficial weeping dermatitis of three years' duration involving the left side of the face and scalp and associated with numer-

31. MacCarty, W. C.: Identification of the Cancer Cell, J. A. M. A. **107**: 844-845 (Sept. 12) 1936.

ous lesions of senile keratosis. There was a squamous cell epithelioma of the ear, grade 3. The histologic picture of some of the moist lesions was that of squamous cell epithelioma of grade 2, with edema and vacuolation of some of the cells, so that at first glance extramammary Paget's disease might be thought of. A great many instances of typical and atypical mitosis could be seen (fig. 5). There was little tendency toward formation of giant epithelial cells or of epithelial giant cells. Cases of similar involvement which at first glance resembles extensive seborrheic eczema of the face have been reported.[32]

I have emphasized repeatedly the importance of distinguishing between keratoma senile and verruca senilis and stated that this distinction can readily be made clinically in the majority of cases.[30] Miescher, Häberlin and Guggenheim [33] have emphasized recently, with justification, the difficulty that sometimes may arise in distinguishing clinically between pigmented verruca senilis, senile keratosis and lentigo with or without malignant changes as they occur on the dorsum of the hands of elderly persons. Histologically, however, the majority of these lesions on microscopic examination prove to be verruca senilis. Occasionally, lesions of senile keratosis with increase in melanin pigmentation may show elongation of the rete ridges without evidence of keratinization of individual cells and may develop into basal cell epithelioma. In 90 per cent of the cases of senile keratosis in which malignant change develops, it is definitely squamous cell epithelioma. Not infrequent are cases in which both leukoplakia and senile keratosis are present, thus calling attention to the close relationship of these two conditions. Furthermore, to distinguish between an early lesion of true Bowen's disease and a plaque of senile keratosis at times may be impossible either clinically or pathologically. Cornu cutaneum is simply a variant of senile keratosis.

ARSENICAL KERATOSIS

Arsenical keratosis and epithelioma independent thereof or arising therefrom have been discussed in a previous paper.[34] In 20 per cent or more of the cases of keratosis epithelioma develops, again starting out as squamous cell epithelioma in situ with various phenomena of keratinization of individual cells. The histologic changes duplicate those

32. Montgomery.[21a] Montgomery and Dörffel.[30b]

33. Miescher, G.; Häberlin, L., and Guggenheim, L.: Ueber fleckförmige Alterspigmentierungen: Ihre Beziehungen zur melanotischen Präcancerose und zur senilen Warze, Arch. f. Dermat. u. Syph. **174**:105-125 (May 15) 1936.

34. Montgomery, H.: Arsenic as an Etiologic Agent in Certain Types of Epithelioma: Differential Diagnosis from, and Further Studies Regarding, Superficial Epitheliomatosis and Bowen's Disease, Arch. Dermat. & Syph. **32**:218-236 (Aug.) 1935.

in cases of Bowen's disease and senile keratosis. In addition, there may be a peculiar type of vacuolation of the cells of the epidermis. Anderson still maintained in his last publication [35] that both Bowen's disease and superficial epitheliomatosis are predominantly the result of ingestion of arsenic, whether or not such a history can be obtained. Franseen and Taylor [36] failed to distinguish between superficial epitheliomatosis and superficial epithelioma developing after the ingestion of arsenic and thus, I believe, erroneously reported many cases of basal cell epithelioma as attributable to arsenical medication. Neither author has attempted to demonstrate arsenic in the tissue by histochemical or quantitative chemical determinations. Further observations merely have confirmed statements that I made earlier, that in order to attribute epithelioma or keratosis to arsenic more arsenic should be demonstrable in the tumor than in the surrounding normal epidermis. I agree with Fischer-Wasels [37] that the administration of inorganic or pentavalent arsenic may accelerate latent or dormant cutaneous malignant foci of the skin. Thus, in a case in which there is a tendency for superficial epitheliomatosis to develop, the process may be accelerated, and basal cell epithelioma in the process of formation may be present together with arsenical keratosis and an arsenical type of epithelioma. It is when both types of epithelioma occur at the same time that confusion results.

Many patients may take arsenic in various forms without having keratosis or pigmentation develop; or they may have involvement of the liver or other organs. Therefore, the question of individual sensitivity or susceptibility to arsenic must be considered. Keratoses resulting from arsenic may develop for the first time twenty or thirty years after the arsenic has been administered. Conversely, cases have been reported in which after discontinuation of arsenic the pigmentation and even the arsenical keratosis have involuted. This is comparable to the reversible reaction cited by Bloch [1] for experimental carcinoma and by Schürch [38] for experimental roentgen ray keratosis. Schürch emphasized that involution of the keratosis does not occur when frank histo-

35. Anderson, N. P.: Arsenical Keratoses of the Palms and Soles; Prickle Cell Epithelioma of a Finger; Multiple Benign Superficial Epithelioma, Arch. Dermat. & Syph. **35**:323-324 (Feb.) 1937.

36. Franseen, C. C., and Taylor, G. W.: Arsenical Keratosis and Carcinomas, Am. J. Cancer **22**:287-307 (Oct.) 1934.

37. Fischer-Wasels, B.: Experimentelle Grundlagen und Folgerungen der Regenerations-theorie der Geschwulstbildung, Klin. Wchnschr. **11**:1937-1941 (Nov. 19); 1977-1982 (Nov. 26) 1932. The Origin of Cancer, editorial, J. A. M. A. **102**:214-215 (Jan. 20) 1934.

38. Schürch, O.: Studien über Präcancerosen mit besonderer Berücksichtigung des experimentellen Röntgencarcinoms, Ztschr. f. Krebsforsch. **33**:1-75 (Aug. 2) 1930.

logic evidence of malignant change is present. I believe that Bowen's disease and superficial epitheliomatosis should not be confused with arsenical keratosis or superficial epithelioma arising therefrom.

KERATOSES RESULTING FROM RADIOTHERAPY OR CONTACT WITH VARIOUS TYPES OF TAR

Excluding the mild type of radiodermatitis, grade 1, in which epitheliomatous change rarely occurs, in at least 19 per cent of cases radiodermatitis shows malignant change.[39] This starts as keratosis or as superficial epithelioma, and in the majority of cases there is definite morphologic evidence of origin as squamous cell epithelioma in situ. Again, keratosis experimentally produced with roentgen rays reveals a histologic picture simulating that of Bowen's disease, and the borderline between benign and malignant epithelial changes is not a sharp one pathologically. This also is especially true of keratosis resulting from contact with tar, produced among experimental animals. The histologic picture of tar-produced cancer, whether occurring among human beings [40] or among animals,[41] frequently shows changes similar to those seen in Bowen's disease beginning as squamous cell epithelioma in situ.

LEUKOPLAKIA

The incidence of epitheliomatous change in leukoplakia is difficult to ascertain because of the various etiologic factors to be considered. McCarthy [42] justly emphasized that the leukoplakia precipitated by syphilis predominates on the tongue, where atrophic syphilitic glossitis is most frequently the antecedent lesion. Leukoplakia of the buccal surfaces, on the other hand, apparently results most frequently from

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39. Montgomery, H.: Pathologic Histology of Radiodermatitis, in MacKee, G. M.: X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1938, chap. 24, pp. 333-362. Saunders, T. S., and Montgomery, H.: Chronic Roentgen and Radium Dermatitis: An Analysis of Two Hundred and Fifty-Nine Cases, J. A. M. A. **110**:23-28 (Jan. 1) 1938.

40. (*a*) Miescher, G.: Hautkrebs und Krebsforschung, Schweiz. med. Wchnschr. **64**: 979-985 (Oct. 27) 1934; abstracted, Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1935, pp. 550-553. (*b*) Shambaugh, P.: Tar Cancer of the Hip in Fishermen, J. A. M. A. **104**:2326-2329 (June 29) 1935.

41. Guldberg, G.: Experimental Researches on Precancerous Changes in the Skin and Skin Cancer: Investigation of Local Action of Tar on the Skin and Its Different Elements, Acta path. et microbiol. Scandinav., 1931, supp. 8, pp. 7-209; abstracted, Arch. Path. **14**:579-581 (Oct.) 1932. Seelig, M. G., and Cooper, Z. K.: A Review of the Recent Literature of Tar Cancer (1927-1931 Inclusive), Am. J. Cancer **17**:589-667 (March) 1933. Schürch.[38]

42. McCarthy, F. P.: Etiology, Pathology and Treatment of Leukoplakia Buccalis with a Report of Three Hundred Sixteen Cases, Arch. Dermat. & Syph. **34**:612-623 (Oct.) 1936.

constant irritation and trauma from smoking or malocclusion. An analysis of different statistics given by MacKee and Cipollaro [21d] together with a review of the literature showed that in 20 or 30 per cent of cases leukoplakia of the oral cavity results in malignant change. I can see no difference between leukoplakia or leukokeratosis of the mucous membranes of the mouth and of those of the genitalia, including the vulva and glans penis.[21b] Erythroplasia of Queyrat [43] would seem at best only a variant of leukoplakia, being essentially a moist superficial form of the latter. Rejtö's [44] case of erythroplasia of the glabrous skin was an instance simply of moist superficial squamous cell epithelioma. The histologic changes in leukoplakic vulvitis, as distinguished from those of true kraurosis and lichen sclerosus et atrophicus (which has been confused with kraurosis [45]), need not be considered here. I have not been able to demonstrate pathologically any evidence of syphilis in cases of leukoplakic vulvitis. The incidence of epitheliomatous changes in lesions of leukoplakia of the genitalia in my experience has been at least 20 per cent, but if the patients are observed over a long period, as Taussig [46] has done, the incidence of epitheliomatous change may reach 50 per cent. Clinically, as in experimental production of cancer, involution of early leukoplakic lesions in the mouth or on the tongue may be seen after cessation of smoking or the fitting of proper dentures, thus again indicating the reversibility of the process if it has not gone too far.[47]

In contrast with the previously mentioned types of precancerous dermatosis, leukoplakia of the mucous membranes, although frequently starting as an epithelioma in situ, may be seen often in the form of an ordinary type of penetrating squamous cell epithelioma, grade 1 to 4, without much evidence of malignant dyskeratosis or keratinization of individual cells.

ETIOLOGIC FACTORS IN PRECANCEROUS DERMATOSES

In the general group of precancerous dermatoses with similar histologic pictures there are (1) true Bowen's disease without any known

43. Stiles, F., Jr.: Erythroplasia of the Glans Penis (Queyrat), Arch. Dermat. & Syph. **30**:647-650 (Nov.) 1934. Sulzberger, M. B., and Satenstein, D. L.: Erythroplasia of Queyrat, ibid. **28**:798-806 (Dec.) 1933.

44. Rejtö, K.: Gemeinsames Vorkommen von Basalioma cutis superficiale planum und Erythroplasia Queyrat, Dermat. Wchnschr. **103**:1125-1131 (Aug. 15) 1936.

45. Hunt, E.: Leucoplakia Vulvae, Kraurosis Vulvae, and Lichen Planus of the Vulva, Brit. J. Dermat. **48**:53-84 (Feb.) 1936.

46. Taussig, F. J.: Leukoplakia and Cancer of the Vulva, Arch. Dermat. & Syph. **21**:431-445 (March) 1930.

47. Ullmann, K.: Ueber Leukoplakien und Krebsbildung in den verschiedenen Schleimhautgebieten: Vorläufiger Bericht über eine vergleichende Studie, Wien. med. Wchnschr. **85**:456 (April 20); 488 (April 27) 1935.

cause, (2) senile keratosis in which actinic rays and senile cutaneous changes may be precipitating factors, but only when the lesions occur on the exposed surfaces of the body, (3) arsenical keratoses resulting from ingestion internally of a carcinogenic substance (arsenic), (4) occupational cancer resulting from a local irritating effect of a carcinogenic substance (tar), (5) keratoses resulting from the irritating effect of exposure to actinic waves of various wavelengths during radium and roentgen therapy, the rays of which are known to be carcinogenic, and (6) leukoplakia resulting from repeated trauma, irritation and chronic inflammatory changes due to various causes. It is surprising that despite the varied predisposing etiologic factors all these conditions should reveal similar evidence of epitheliomatous changes in about 20 per cent of the cases. The well known and accepted role of actinic rays in the production of epithelioma [48] is applicable only to senile keratosis and that resulting from radiation and, as mentioned previously, to the different phenomena seen in lesions of xeroderma pigmentosum.

SO-CALLED PRECANCEROUS DERMATOSIS

Under the term "precancerous dermatosis" have been grouped a great many cutaneous diseases in which the incidence of epitheliomatous change is no greater than would be expected when the age of the subject and various factors which tend to predispose to carcinoma are taken into consideration. Thus, verruca senilis has been confused clinically and pathologically with senile keratosis.[49] Epithelioma actually developed in less than 2 per cent of the cases of verruca senilis (seborrheic keratosis) and then only in lesions that had been subjected to prolonged trauma and irritation.[30a] Any lesion of epithelial hyperplasia when subjected to prolonged trauma and irritation or recurrent infection may eventuate in epithelioma under suitable circumstances. This, in my experience is also true of pigmented nevi,[18b] lentigenes,[50] various types of syphilitic lesions and chronic ulcers, especially varicose ulcers, but the incidence of true malignant change is relatively low. The incidence of epithelioma arising in or from sebaceous cysts is between 2 and 9 per cent.[51] Most cases of psoriasis and epithelioma reported

48. Körbler, J.: Das Sonnenlicht in der Aetiologie der Hautkarzinome, Strahlentherapie **52**:353-358, 1935.

49. Geschickter, C. F., and Koehler, H. P.: Ectodermal Tumors of the Skin, Am. J. Cancer **23**:804-836 (April) 1935. Rosenberg.[20]

50. Zeisler, E. P., and Becker, S. W.: Generalized Lentigo: Its Relation to Systemic, Nonelevated Nevi, Arch. Dermat. & Syph. **33**:109-125 (Jan.) 1936.

51. Bishop, E. L.: Epidermoid Carcinoma in Sebaceous Cysts, Ann. Surg. **93**:109-112 (Jan.) 1931. Stone, M. J., and Abbey, E. A.: Sebaceous Cyst: Its Importance as a Precancerous Lesion, Arch. Dermat. & Syph. **31**:512-515 (April) 1935.

in the literature were instances of epithelioma independent of the psoriatic patches, although epitheliomatous changes in a psoriatic patch and independent of arsenical medication have been described.[52] The rare occurrence of epitheliomatous changes in many other lesions of benign dermatoses independent of previous therapy might be mentioned.[53]

There have been numerous reports regarding the incidence of malignant change in tuberculous lesions of the skin, especially lupus vulgaris. This apparently varies from 0.5 per cent to as high as 4 per cent in a series of cases, including many cases in which intensive actinotherapy of various types was employed.[54]

Veiel [55] found the occurrence of epithelioma to be less frequent in lupus erythematosus than in lupus vulgaris. Analysis of reports of cases of lupus erythematosus in which epitheliomatous changes had occurred [56] revealed that the epithelioma had developed in 6 to 12 per cent of these cases without any treatment having been given, in contrast to its appearance in 20 to 30 per cent of cases after radiotherapy had been instituted. The relative frequency of epithelioma reported in cases of lupus erythematosus in which no radiotherapy is given may be explained by the relatively frequent occurrence of the disease on the face in the later decades of life. When lesions of lupus erythematosus occur on the exposed surfaces, there are distinct degenerative changes histologically in the elastic and connective tissue, resulting in merging of the two types of fibers and in changes comparable to those seen in senile skin or so-called sailor's skin. It is a well established fact that epitheliomatous changes are more frequently encountered among persons who have this weather-beaten type of skin and who are exposed to the

52. Alexander, A.: Carcinomentwicklung auf psoriatischer Basis, Arch. f. Dermat. u. Syph. **129**:5-13, 1921. Wright, C. S., and Friedman, R. J.: Psoriasis and Multiple Superficial Epithelioma, Arch. Dermat. & Syph. **27**:70-77 (Jan.) 1933.

53. Isaak: Fall zur Diagnose, Dermat. Wchnschr. **94**:664 (May 7) 1932; Acrodermatitis chronica atrophicans + Sklerodermie, Karzinom am Unterschenkel, ibid. **94**:664 (May 7) 1932; abstracted, Cancer Rev. **7**:473 (Dec.) 1932.

54. Truffi, G.: Neoplasie maligne su lupus, Arch. ital. di dermat., sif. **9**:443-542 (Oct.) 1933; abstracted, Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1935, pp. 301-302. Volk, R.: Tuberculose der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1, pp. 1-686.

55. Veiel, F.: Lupus erythematodes (Cazenave), in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1, pp. 687-795.

56. Tischnenko, A. M.: Contribution à l'étude de la pathogénie du carcinome d'origine érythémato-lupique, Ann. de dermat. et syph. **3**:708-727 (Aug.) 1932. Uhlmann, E., and Schambye, G.: Lupus erythematosus und Carcinom, Arch. f. Dermat. u. Syph. **170**:500-510 (Sept. 14) 1934.

weather and to the sun.[57] In cases of both lupus vulgaris and lupus erythematosus, with few exceptions, when malignant changes occur they are squamous cell rather than basal cell epithelioma. Occasionally sarcomatous changes have been observed. Few of the lesions have been described as beginning as squamous cell epithelioma in situ.

Arndt [58] found that in 1 to 1.5 per cent of cases carcinoma of the skin involved the extremities and in 9 per cent of these developed in burns, sometimes not until a great many years had elapsed. Repeated trauma apparently played a prominent role. The great majority of these lesions were frank invading squamous cell epithelioma. There was little evidence of keratinization of individual cells or Bowen-like changes. The long interval between the development of the burn and the occurrence of epitheliomatous change parallels that in cases of occupational epithelioma resulting from dyes, roentgen rays or tar, in which intervals of seven to fifteen years frequently occur.[59] That 9 per cent of the scars from burns result in epitheliomatous change might be anticipated when the age of the patient, the factor of impaired circulation and liability of the scars on the legs to repeated trauma are taken into consideration. It is likely that similar figures will be available in the future in regard to ulcers or scars from other causes. In these cases of so-called precancerous dermatosis the incidence of epitheliomatous change did not approximate that in those conditions to which I would limit the term.

PSEUDOEPITHELIOMATOUS HYPERPLASIA

Reference must be made briefly to various types of granuloma, especially blastomycosis, bromoderma, iododerma, sporotrichosis, actinomycosis, tularemia and various chronic forms of tuberculosis and syphilis of the skin in which an extreme degree of pseudoepitheliomatous hyperplasia may be seen.[60] This usually simulates ordinary penetrating squamous cell epithelioma, grade 1 to 3. There rarely is any evidence of squamous cell epithelioma in situ with the phenomenon of keratinization of individual cells. Dunn and Smith [61] mentioned self healing of a malignant squamous cell epithelioma which from their histologic descrip-

57. Miescher.[40a] Körbler.[48]

58. Arndt, G.: Ueber den Brandnarbenkrebs und das symmetrische Karzinom der Extremitäten, Beitr. z. klin. Chir. **157**:305-332, 1933.

59. Wells, H. G.: The Nature and Etiology of Cancer, Am. J. Cancer (supp.) **15**:1919-1968 (July) 1931.

60. Montgomery, H., and Holman, J. C., Jr.: Pseudo-Epitheliomatous Hyperplasia in a Case of Sporotrichosis, Proc. Staff Meet., Mayo Clin. **13**:465-469 (July 27) 1938. White, C., and Weidman, F. D.: Pseudo-Epitheliomatous Hyperplasia at the Margins of Cutaneous Ulcers, with Especial Reference to Histologic Diagnosis, J. A. M. A. **88**:1959-1963 (June 18) 1927. Broders.[8]

61. Dunn, J. S., and Smith, J. F.: Self-Healing Primary Squamous Carcinoma of the Skin, Brit. J. Dermat. **46**:519-523 (Dec.) 1934.

tions and illustrations could at most have been low grade squamous cell epithelioma, of grade 1, but which from their clinical description suggested bromoderma with pseudoepitheliomatous hyperplasia.[62] To distinguish between pseudoepitheliomatous hyperplasia and squamous cell epithelioma at times may be difficult.

COMMENT

The term "precancerous dermatosis" is difficult to define. Bloch [1] quoted Schürch [38] as follows:

> As long as we do not know the biochemical changes which characterize the cancer cell and differentiate it from the normal mother-cell, we shall be unable to know wherein lies the essential characteristic of a precancerous change, or, in other words, the problem of an unequivocal differentiation of precancerosis is at present insoluble.

Bloch stated that the concept of precancerous dermatosis is partly clinical and statistical and partly morphologic and histologic. He emphasized the common histologic characteristics of epithelioma in situ and stated that the term "precancerous dermatosis" should be applied to those cutaneous conditions which if left alone would in a large but not yet exactly fixed percentage of cases sooner or later, sometimes only after a long time, turn into actual cancer. It is now possible, I believe, to confirm Bloch's concept and to state that most of the conditions which he included under the term "precancerous dermatosis" will in 20 per cent or more of cases show malignant change and that they all have a common pathologic picture of squamous cell epithelioma which begins, as a rule, in situ, with the phenomena of malignant dyskeratosis and keratinization of individual cells. The incidence of epitheliomatous change in this type of precancerous dermatosis is from two to twenty times greater than that associated with various benign dermatoses that frequently have been referred to in the past as precancerous.

Use of the term "precancerous" has been criticized, repeatedly most recently by Sutton [63] and by Hellwig.[64] Hellwig said:

> "Precancer" as a histologic diagnosis is meaningless . . . the pathologist should take the full responsibility by pronouncing the lesion malignant or benign

62. Goeckerman, W. H.: Iododerma and Bromoderma, Minnesota Med. **12:** 408-413 (July) 1929.

63. Sutton, R. L., Jr.: Early Cutaneous Carcinoma, J. A. M. A. **104**:433-439 (Feb. 9) 1935; Pathologic and Clinical Aspects of Early Skin Carcinoma, J. Missouri M. A. **32**:224-227 (June) 1935; Carcinoma of the Skin in Its Early Manifestations: A Correlation of Clinical and Microscopic Observations with the Hypothesis of Etiology in Somatic Mutation, South. M. J. **29**:235-238 (March) 1936; Potential Malignancy of Small Skin Lesions, J. Kansas M. Soc. **38**:97-100 (March) 1937.

64. Hellwig, C. A.: The Scientific Basis of Biopsy in Tumors, Arch. Path. **14**:517-554 (Oct.) 1932.

. . . Nothing is gained by calling a suspicious change in the tissue a precancerous lesion, a term which is a confession of ignorance.

In the same article, however, he pointed out that many epitheliomas of the bladder which Broders classified as of grade 1 are tumors that most pathologists would call benign papillomas. Sutton dwelt on Hansemann and Whitman's concept of somatic mutation of the cancer cell and stated that definite cancer cells may be present histologically in a lesion and yet the lesion (fundamentally a carcinoma) may run a benign clinical course throughout the lifetime of the patient. I agree with Broders [8] and Sutton in supporting Hansemann and Whitman's concept of somatic mutation. I also agree with Savatard [19] that in cases of epithelioma in situ the cancer may be spread through metaplasia of adjacent normal cells rather than by penetration of the tumor into the surrounding healthy epidermis. In most of Sutton's cases, however, definite clinical as well as pathologic evidence of epithelioma was already present. I have tried to show in this article and in the illustrations that when the earliest changes are present, all stages of transition histologically between a benign and a malignant process are seen. Furthermore, as Hellwig stated, and probably correctly, if many pathologists would not agree in distinguishing between benign papilloma and squamous cell epithelioma of grade 1 there would obviously be wider divergence of opinion regarding early epitheliomatous changes in situ in this group of precancerous dermatosis. I might cite other evidence to show transitions from benign to malignant neoplasms. Thus, in cases of Kaposi's sarcoma the original lesion histologically is a benign inflammatory process of the reticuloendothelial system which eventuates in frank malignant sarcoma with metastasis.[65] The same thing is true of transitions seen in various forms of lymphoblastoma from mycosis fungoides and leukemia to lymphosarcoma.[66] Even in cases of basal cell epithelioma a sharp distinction cannot always be made between a benign and a malignant process.[18b]

The limitations of a diagnosis based on morphologic histologic changes alone must be recognized, but when these are correlated with the clinical findings and course of the disease, the concept of true Bowen's disease, senile keratosis, keratosis resulting from arsenic, tar or radiotherapy and various forms of leukoplakia as precancerous dermatoses seems justifiable. Because of the tendency in all these conditions toward development of histologic changes similar to those

65. Dörffel, J.: Histogenesis of Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi, Arch. Dermat. & Syph. **26**:608-634 (Oct.) 1932.

66. Montgomery, H.: Mycosis Fungoides, Lymphoblastoma of the Skin, and Allied Conditions as General Diseases, in Christian, H. A., and Mackenzie, J.: Oxford Loose-Leaf Medicine, New York, Oxford University Press, 1936, vol. 4, chap. 1A, pp. 1-19.

of early epithelioma developing from radiodermatitis, it seems illogical to subscribe to the prevalent practice of treating these conditions with roentgen rays or radium.[67] Mottram,[68] in studying production of epithelial tumors, showed that mice with precancerous lesions had a greater number of epidermal tumors after application of gamma radiation in doses of about 1,000 roentgens, or insufficient to destroy the epidermis, than when radiation was not used. In other words, if good results are to be expected from radiotherapy in cases of precancerous dermatosis which histologically already shows malignant change, intensive destructive doses must be used. Destruction by surgical excision, including endothermy or actual cautery, is the method of choice.

CONCLUSIONS

In the group of precancerous dermatoses are included true Bowen's disease, senile keratoses, keratoses resulting from arsenic, tar or radiation and leukoplakia of the mucous membranes. In 20 per cent or more of the cases, epithelioma of varying degrees of malignancy eventually will develop, usually starting as squamous cell epithelioma in situ. The conditions are all interrelated by their common histologic picture and, hence, a possible common carcinogenic factor. They are not to be confused with the relatively rare epithelioma in lesions of lupus vulgaris or other benign dermatoses, such as psoriasis and lichen planus. Precancerous dermatoses also must be distinguished from various conditions which result in the histologic picture of pseudoepitheliomatous hyperplasia. The incidence of epithelioma associated with lupus erythematosus or with scars from burns or other causes will vary up to 10 per cent in cases of such involvement, but senile cutaneous changes, the age of the patient, the situation of the lesions, including the factors of repeated trauma and irritation, and the previous treatment employed must be considered. In many cases of precancerous dermatosis, histologic transitions between a benign and a malignant process may be seen in the same section.

The peculiar or distinctive and predominant histologic feature of epithelioma in situ with the phenomena of Bowen's disease, together with their relatively long duration as such, without clinical or histologic evidence of malignant invasion, I believe, justify the grouping of true Bowen's disease, senile keratosis, keratosis resulting from arsenic, tar and radiation and in most cases leukoplakia of the mucous membranes under the title "precancerous dermatosis." If the term "pre-

67. Molesworth, E. H.: Cancer in the Movies: A New Movie Menace, Arch. Dermat. & Syph. **31**:231-233 (Feb.) 1935.

68. Mottram, J. C.: Production of Epithelial Tumors by Irradiation of a Precancerous Lesion, Am. J. Cancer **30**:746-748 (Aug.) 1937.

cancerous dermatosis" is used in the limited sense that I have defined, it has a definite meaning both clinically and pathologically and is of value from the standpoint of prognosis and treatment until more is known about the cause of cancer. The term "precancerous dermatosis," however, should not be used loosely when the pathologist is in doubt regarding the clinical or histologic picture, despite the fact that at present there is no general agreement regarding the distinction between cancer and precancerosis of the skin.[69]

69. Since this paper was written, R. L. Sutton Jr. (Early Epidermal Neoplasia: Description and Interpretation; the Theory of Mutation in the Origin of Cancer, Arch. Dermat. & Syph. **37**:737-780 [May] 1938) has advanced the theory that cancer probably begins in a solitary cell and that neoplastic lesions of the epidermis may be classified according to the coherence of the cells and the rapidity of their growth and has stated that this theory does away completely with the concept of "precancerosis." The coherence of epitheliomatous cells, in my experience, however, is dependent, in part at least, on the degree of vascularity, the lymphatic stasis and the inflammatory reaction present in a lesion. A venereal wart or a lesion of Darier's disease may show little coherence of the cells and a rapid rate of growth, as evidenced by numerous mitotic figures, in contrast with squamous cell epithelioma, grade 3 or 4, in which narrow strands of tumor cells are present but still adherent to one another and possessing a variable number of atypical mitotic figures. I agree with Sutton that the benign or malignant character of a solitary lesion or the degree of malignant change that may develop in the future cannot be accurately predicted either clinically or pathologically. A tiny lesion of senile keratosis with an inflammatory areola may histologically be squamous cell epithelioma, whereas in other instances multiple relatively large senile keratoses without an inflammatory areola may histologically show little evidence of either benign or malignant dyskeratosis. Hence, there is importance in considering the patient and his susceptibility to the unknown etiologic factors of cancer rather than basing analysis on individual lesions. I have studied specimens from several hundred lesions of precancerous dermatosis of different types, especially in the earliest stages, including more than 100 specimens of senile keratoses, in which the incidence of epithelioma remained at 20 to 25 per cent, in contrast with an incidence of less than 2 per cent in most types of benign dermatoses. The theory of mutation in the origin of cancer does not deny the concept of precancerous dermatosis, but simply tends to explain epithelioma in situ. According to my experience with both basal cell epithelioma and squamous cell epithelioma in situ, one is more likely to see evidence of multicentric points of origin in the epidermis than evidence of epithelioma developing from a solitary cell. In all of Sutton's illustrations there is evidence of frank malignant change, easily diagnosed as such. I cannot see the value of classifying epidermal neoplasms on the basis of coherence of the cells rather than by the generally accepted method of classification and grading employed by Broders.

MAL DE MELEDA

REVIEW OF THE LITERATURE AND REPORT OF FOUR CASES

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Mal de Meleda receives its name from the Dalmatian island where it was originally observed.[1] In 1826 Stulli [2] first described this condition, in a letter to the director of anthology in Florence, Italy. Seventy years later, Hovorka reported the disease under the title "Concerning an Heretofore Unknown Endemic 'Lepraherd' in Dalmatia." Later he realized it was not leprosy and with Ehlers [3] used the term mal de Meleda. In 1898 Neumann [4] undertook a study of this disease and emphasized its close relationship to the keratosis of Unna [5] and Thost [6] and to the still earlier reports of Haskel, Behrend, Sommering and Boegehold.

Since Neumann made his report, mal de Meleda has not been studied on the island of Meleda. There have been numerous articles on this subject in the French and German literature, but none have appeared in the American literature within the last five years. We think it timely, therefore, to present a short review of this disease and to report 4 cases which recently have come to our attention.

Among cases of mal de Meleda have been included cases of hereditary palmar and plantar keratoderma, endemic in the island of Meleda but also seen elsewhere, in which the hyperkeratosis is not confined to the palms and soles but occurs also on other parts of the body in circumscribed patches, and in which the disease is inherited

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1. Moncorps, C., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 5, pt. 2, p. 300.

2. Stulli, cited by Moncorps.[1]

3. Hovorka, O., and Ehlers, E.: Mal de Meleda, Arch. f. Dermat. u. Syph. **40**:251, 1897; cited by Moncorps.[1]

4. Neumann, I.: Ueber Keratome hereditarium, Arch. f. Dermat. u. Syph. **42**:163, 1898; cited by Moncorps.[1]

5. Unna, P. G.: Ueber das Keratoma palmare et plantare hereditarium, Vrtljschr. f. Dermat. **10**:231, 1883; cited by Moncorps.[1]

6. Thost: Ueber erbliche Ichthyosis palmaris et plantaris, Inaug. Dissert., Heidelberg, 1880; cited by Moncorps.[1]

as an irregularly dominant (or recessive) trait. This condition has been referred to by the following synonyms: keratoma hereditarium (Neumann [4]), keratoma palmare et plantare hereditarium (Unna [5]), congenital ichthyosis palmaris et plantaris (Thost [6]) and *kératodermie familiale* (Darier [7]). Moncorps expressed preference for the simple term "keratoses."

CLINICAL PICTURE

Typically this disease appears within the first two years of life, usually at about the sixth month. Redness of the palms and soles is the first manifestation, soon followed by roughening and thickening. Winkle [8] described a bluish red line about 0.5 cm. wide at the dorsopalmar junction as an initial symptom in a 4 month old girl. Finally, the palms and soles are covered by a thick horny layer. This is bordered by a bluish red zone about 1 cm. wide, which completely surrounds the hyperkeratosis, extending to the dorsal aspects of the webs of the fingers and toes and the flexures of the wrists. On the feet the involvement may end at or extend up over the achilles tendon. The clinical picture may vary from massive transparent yellowish hyperkeratosis with the patterns of the papillary body still intact to extremely marked hyperkeratosis with many fissures and a heaped-up greenish black horny layer. There is usually associated local hyperhidrosis, and when this is present one notices, deep in the fold, a succulence of the horny layer due to mechanical inhibition of the flow of perspiration. In association with this, the palms and soles give off a fetid odor like that of rancid butter. In a typical case there are few if any scales, and attempts to pull off loose skin cause pain.

In mal de Meleda other areas are usually involved. One often finds circumscribed areas of hyperkeratosis on the internal malleoli, on the extensor surfaces of the knees and elbows, in the axillas,[1] on the dorsa of the hands and occasionally on the trunk.[9] Abnormalities of the nails have been observed, the most frequent of which are thickening, transverse ridging, clawlike convexity (case 2) and subungual hyperkeratosis, while onychogryphosis and longitudinal stripes are more rare. Associated leukoplakia and leukokeratosis have also been noted.

The symptoms are due largely to the mechanical interference with flexibility and sensibility to touch and to the patient's personality reac-

7. Darier, J.: Précis de dermatologie, Paris, Masson & Cie, 1923; cited by Moncorps.[1]

8. Winkle, T.: Ueber Keratosis hereditarium palmaris et plantaris, Inaug. Dissert., Munich, 1925; cited by Moncorps.[1]

9. Nadel, A.: Keratoma palmare et plantare atypicum, Arch. f. Dermat. u. Syph. **174**:404, 1936.

tions to his deformity. The odor and the roughness of the hands naturally cause great embarrassment. In cases of severe disease the hyperkeratosis produces such shrinking that the hand is held closed (main en griffe—Postowsky [10]).

The disease usually extends for a lifetime. The earlier it appears, the more severe it is likely to be; the later it appears, the more rapid is the evolution, but the less marked it becomes. Occupation and the degree of hyperhidrosis affect the intensity of the disease. Manual labor may convert mild hyperkeratosis into a severe involvement with great thickening. Excessive moisture may enhance secondary infection by fungi or bacteria. In any event, the prognosis is poor, since the disease remains stationary and refractory to treatment. It usually reaches its height about ten years after onset. Occasionally it becomes less intense after this. In later years the erythematous border may disappear entirely, while the lesions on the dorsal aspect of the hands may not be noticed until several years after birth. Instances of spontaneous remission during pregnancy and of complete disappearance of the disease have been reported.[1]

HISTOLOGIC FEATURES

The histologic changes are confined chiefly to the epidermis. There is marked acanthosis; the rete pegs are plump and of uniform length but four to five times as long as normal, and the papillary bodies are smaller. The stratum corneum is greatly thickened and is the site of the most marked histologic changes. The stratum lucidum is also increased, while the stratum granulosum is thicker over the rete pegs than over the papillary bodies. The sweat glands are usually twice their normal size.[1]

ETIOLOGY

Mal de Meleda is a hereditary idiopathic disease, and its occurrence depends little, if at all, on environmental factors. It is inherited as an irregularly dominant or recessive trait and frequently skips generations.[11] Whether consanguinity, the incidence of which is exceedingly

10. Postowsky, D.: Zur Frage der Aetiologie der hereditären symmetrischen Keratodermie, Acta dermat.-venereol. **11**:305, 1930; cited by Moncorps.[1]

11. (*a*) Coulon and Payenneville: Un cas de maladie de Méléda, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **40**:1158, 1933. (*b*) Tappeiner, S.: Zur Klinik der idiopathischen diffusen palmoplantaren Keratodermien, Arch. f. Dermat. u. Syph. **175**:453, 1937; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **5**:612, 1937; abstracted, Wise, F., and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1937, p. 246. (*c*) Siemens, H. W., and Winkle: Ueber regelmässiges Dominanz und andere Vererbungsmodi bei Keratosis palmaris et plantaris (Verhornung der Haut- und Fussflächen), Sitzungsb. d. Gesellsch. f. Morphol. u. Physiol. **36**:45, 1925; cited by Moncorps.[1] (*d*) Moncorps.[1]

high on the island of Meleda, has any direct etiologic relationship is not known. It is certain that consanguinity may cause combination of two recessive inheritance traits, with the result that the incidence is increased and the mode of inheritance may make it appear to be a dominant trait.

There seems to be no constant involvement of any other organ of the body, and when such involvement occurs it is to be regarded as coincidental.[12] Cases have been reported in which there has been coexisting syphilis,[13] hyperthyroidism [14] and vitiligo.[15] These have failed to convince us of an etiologic relationship. In those cases in which the coexisting disorder was treated, the hyperkeratosis usually remained unchanged.

DIFFERENTIAL DIAGNOSIS

The diagnosis is made chiefly from the clinical features. Mal de Meleda may be differentiated from other forms of hyperkeratosis by the family history and the early onset, a factor which is usually absent in occupational or other types of acquired "symptomatic" hyperkeratosis, such as that due to arsenic. The skin in ichthyosis is usually dry and brittle, while in hyperkeratosis it is more flexible and often succulent. Although ichthyosis is inherited, it is not always of the same type, while the type of mal de Meleda is constant in a family. Bettman [16] stated that he had never heard of or observed a case of keratoma hereditarium in a family subject to ichthyosis.

TREATMENT

Treatment is unsatisfactory, and it is impossible to obtain complete and permanent cure, but many local measures, such as the application of peeling ointments and softening of the horny layer by hot soap soaks followed by friction with pumice stone, have been found helpful. Surgical measures such as curettage [17] and sympathectomy [18] have been

12. Günther, H.: Beobachtungen von Keratoma hereditarium palmoplantare (Typus Unna), Arch. f. Dermat. u. Syph. **165**:475, 1932.

13. Nicolas, J., and Rousset, J.: Maladie de Méléda chez deux sœurs hérédo-syphilitiques, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Lyon) **43**: 8, 1936. Spillmann, L., and Weis: Hyperkératose palmo-plantaire bilatérale et symétrique congénitale, ibid. (Réunion dermat.) **40**:10, 1933.

14. Basch, G.; Abraham, and Siguier, F.: Kératodermie palmo-plantaire héréditaire et familiale (maladie de Méléda), Bull. Soc. franç. de dermat et syph. **41**:945, 1934.

15. Kienzler, L.: Keratoma palmare et plantare hereditarium im Korrelation mit anderen, keimplasmatisch bedingten Anomalien, Dermat. Wchnschr. **103**:1630, 1936.

16. Bettman, S.: Ueber die Vererbung von Hautanomalien, Verhandl. d. naturh.-med. Ver. zu Heidelberg **11**:301, 1912; cited by Moncorps.[1]

17. Pels: Keratosis Palmaris et Plantaris; Hyperhidrosis, Arch. Dermat. & Syph. **16**:643 (Nov.) 1927; cited by Moncorps.[1]

18. Giese, E.: Keratodermie symmetrica palmaris et plantaris, Zentralbl. f. Haut- u. Geschlechtskr. **21**:699, 1926; cited by Moncorps.[1] Pels.[17]

useless. Organotherapy [19] with preparations of thyroid, ovary and pituitary and intravenous injections of sodium thiosulfate and sodium salicylate [20] have produced improvement in occasional cases but have failed in others.

In the majority of cases reported application of roentgen rays and of radium had no effect, but Uhlmann [21] and Herrmann [22] reported good results with filtered roentgen rays. Chantriot [23] obtained marked improvement after regional irradiation of the sympathetic nerve fibers of the skin according to the method of Gouin. The keratosis disappeared two months after a dose which produced a strong generalized reaction which was supposed to "stir up" the sympathetic nervous system. How soon it recurred is not mentioned. Konrad [24] reported worth while results with grenz rays. We used roentgen rays in 2 of our cases (1 and 2). In 1 case there was definite improvement, but in the other there was no change.

IS MAL DE MELEDA AN ENTITY?

Many authors include mal de Meleda with keratoma palmare et plantare hereditarium of Unna and use the two terms synonymously. We, however, agree with those [25] who consider mal de Meleda a subdivision and an atypical form with constant characteristics which differentiate it from typical keratoma hereditarium palmare et plantare.

Chief among these differences is the mode of inheritance. The Unna type is transmitted as a rule as a dominant trait,[26] while mal de

19. Hart-Drant: Keratosis Palmaris et Plantaris, Arch. Dermat. & Syph. **11**: 554 (April) 1925; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **17**:876, 1925; cited by Moncorps.[1] Lereboullet and Halle: Kératodermie palmo-plantaire, Bull. Soc. de pédiat. de Paris **23**:265, 1925; cited by Moncorps.[1]

20. Throne, B., cited by Moncorps.[1]

21. Uhlmann: Keratosis hereditarium palmaris et plantaris, Zentralbl. f. Haut- u. Geschlechtskr. **30**:564, 1929; cited by Moncorps.[1]

22. Herrmann: Keratoma palmare et plantare hereditarium, Dermat. Wchnschr. **89**:1284, 1929; cited by Moncorps.[1]

23. Chantriot: Kératodermie et irradiation fonctionnelle du sympathique cutané, Bull. Soc. franç. de dermat. et syph. **36**:1258, 1929; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **34**:803, 1930; cited by Moncorps.[1]

24. Konrad: Ichthyosis atypica palmaris durch Bucky's Grenzstrahlen gut beeinflusst, Zentralbl. f. Haut- u. Geschlechtskr. **32**:34, 1929.

25. Hovorka and Ehlers.[3] Neumann.[4] Siemens and Winkle.[11c]

26. Michael, J. C.: Keratoderma Disseminatum Palmaris et Plantaris: Its Mode of Inheritance, Arch. Dermat. & Syph. **27**:78 (Jan.) 1933. Chung, H. L.: Keratoma Palmare et Plantare Hereditarium, with Special Reference to Its Mode of Inheritance as Traced in Six and Seven Generations, Respectively, in Two Chinese Families, ibid. **36**:303 (Aug.) 1937.

Meleda is inherited as a recessive trait.[27] Mal de Meleda was called "transgrediente" by Siemens and Winkle, who recognized it as atypical. In 3 of our 4 cases (1, 2 and 4) the parents had no cutaneous disease, and the onset was sufficiently early to exclude any of the symptomatic forms of hyperkeratosis. In case 2 the parents were second cousins, and the only other member of the family to have the condition was a brother. In case 3 the data on family background were not sufficient to allow us to determine whether the trait was dominant or recessive, although there were other persons with the condition on the paternal side of the family. When we first saw the patient in case 4, when he was 1 year of age, the disease was definitely present. Neither parent on examination by us showed any evidence of hyperkeratosis. The onset of the condition in this case was earlier than in any which we have been able to find reported in the literature. Where there has been a high incidence of intermarriage, as on the island of Meleda, the mode of inheritance is difficult to determine unless a study is carried back over a large number of generations. There has been no such study which is convincing. In spite of intermarriage on that island, the trait has skipped generations, and this supports the conclusion that mal de Meleda is a fundamentally recessive trait.

Another difference is the greater tendency in mal de Meleda for hyperkeratosis to appear on parts of the body besides the palms and soles. This may occur, but less commonly, in keratoma palmare et plantare hereditarium, so that the difference is really a quantitative one. The same is true of the more frequent marked erythematous border extending to the flexures of the wrists and the dorsa of the webs of the fingers.

REPORT OF CASES

CASE 1.[28]—J. S., a girl aged 17, born in the United States, was first seen in private practice by one of us (H. D. N.) on Jan. 28, 1936. Her father was German-Swiss and her mother French, and they were not related. The patient was an only child, and neither of her parents nor any other relative had had any cutaneous disease. Her palms and soles were entirely normal at birth, but when she was 3 weeks old her palms became red, thickened and scaly and her soles began to turn red. After a short time the soles became normal and remained so, but the condition on the palms persisted. The palms never itched or caused any other sensation, but after the onset they persistently gave off a sour odor like that of yeast; this gradually diminished, and the condition improved in other respects. There was a great deal of peeling of the skin of the palms until the patient was 9 years of age, but there has been none since. There was no seasonal variation. Menstruation began at the age of 12 and was normal. The weight

27. Moncorps.[1] Neumann.[4] Siemens and Winkle.[11c]

28. This case was presented at a meeting of the Section on Dermatology and Syphilis of the New York Academy of Medicine on Feb. 4, 1936 (Arch. Dermat. & Syph. **34**:1051 [Dec.] 1936).

was constant and the general health excellent. Between the ages of 2 and 5 years the patient from time to time took a few drops of a solution of arsenic, which caused some improvement.

Examination showed the skin of both palms to be symmetrically involved, and there were a sharply outlined border between the palms and the normal skin at the junction of the palm and the flexor surface of each wrist and in the first interspace of each hand and a fairly sharply outlined pale red border in all the other interspaces. Both palms were slightly moist and gave off a somewhat acid yeastlike odor. The skin of the palms was uniformly thickened and slightly red, but there was no scaling or vesiculation. There was an area of normal skin the size of a finger tip in the upper part of the center of each palm. The finger nails and toe nails were not involved, and the feet were normal except for a considerable amount of fine peeling under all the toes and some hyperhidrosis between the toes. The rest of the skin and hair were normal except for slight dryness and redness of the skin on the lower parts of the legs.

The basal metabolic rate was —14 per cent. Intradermal injections of trichophytin and oidiomycin, examination for fungi, a Wassermann test, urinalysis, twenty-five scratch tests and a general physical examination failed to show any abnormality.

From Feb. 8 to May 9, 1936, the patient received ten treatments of a quarter of an erythema dose (75 r) each of unfiltered roentgen rays to both palms and the dorsa of the interspaces of each hand and from June 5 to Sept. 17, 1936, four additional treatments of the same dose to the dorsum of the first interspace of each hand and three treatments of a quarter of an erythema dose filtered with 3 mm. of aluminum (137.5 r) to each palm. She also took ¾ grain (0.05 Gm.) of thyroid daily from February 8 to April 25, and from the latter date to June 5 she took 9 to 15 drops of a solution of potassium arsenite U. S. P. daily. Since Sept. 25, 1936, she has used occasionally an ointment containing 3 per cent salicylic acid. Improvement started soon after roentgen therapy was begun and became progressively more marked. On May 9, 1936, at the time of the tenth roentgen treatment, the patient stated that her hands had never been better. On that date there was no sweating or odor on the palms; the red border on the wrists was barely visible and that in the first interspaces rather faint, and there was only some fine superficial scaling in patches on the palms. At times, without apparent reason, but especially just before menstruation, the palms became worse for a short time, but they soon became practically normal again. The patient was next seen on Dec. 28, 1937. At that time there was no perspiration or odor on the palms, but the skin of the palms, the flexures of the wrists and the dorsa of the interspaces of the fingers, chiefly the first, was still somewhat thickened and red. The condition as a whole, however, was much better than on her first visit, although she had had no treatment for over a year. For the first time, slight thickening of the skin over one malleolus was noticed.

She was not seen again until June 22, 1938. At this time there was no odor or excessive sweating in either palm, but the skin of both palms was red and thickened, and this change extended to the flexures of the wrists and the dorsa of the interspaces of the fingers. It was most marked on the dorsa of the first interspaces. Since her last visit she had had no treatment except occasional use of the salicylic acid ointment. Since she had had no roentgen treatment for over two years, it was decided to resume that form of therapy, and from June 22 to the date of writing (July 20, 1938), she received five doses of 75 r each of

unfiltered roentgen rays. The erythema and thickening have almost entirely disappeared from all the affected areas. The palms are now of almost normal color, are not moist and have no odor.

CASE 2.[29]—V. B., a girl aged 20, born in the United States, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 15, 1936, because of an eruption on the palms and soles and dystrophy of the nails of fourteen years' duration. Her parents were second cousins, and her father was Sicilian. Both of her parents and four grandparents were living, and neither they nor any of her aunts, uncles or cousins had had any cutaneous disease. One brother had an identical condition of the palms and soles and a sharply marginated eruption on the dorsa of the hands. One sister had died in infancy, and the patient did not know whether her skin was normal. Examination at the time of her first visit revealed great thickening, maceration and yellowish discoloration of the palms and soles, with some scaling and deep fissures in places (figs. 1 and 2). The eruption extended to the sides of the feet and between the toes and to the dorsa of the interspaces of the fingers (fig. 3) and the flexor surfaces of the wrists. The border was sharply defined, slightly elevated, brownish red and scaly. The palms and soles gave off a sour odor. There was much maceration between the toes. The finger nails showed thickening, transverse ridging and clawlike convexity. There was a yellowish olive-sized nodule over the internal and the external malleolus of each ankle (fig. 4).

When this patient was presented by Dr. Fraser before the New York Dermatological Society, Drs. H. H. Whitehouse, G. M. MacKee and Fred Wise agreed with the diagnosis of mal de Meleda.

Histologic examination of a biopsy specimen taken from the right sole showed marked hyperkeratosis. The horny layer was more than twice as thick as the rest of the epidermis and cutis combined (fig. 5). Three examinations of the urine showed no abnormality, and a Wassermann test of the blood was negative. On her first visit, scrapings from the right sole showed several hyphae, but no fungi appeared on examination of specimens from the left sole, the nails and the palms. Subsequent examinations failed to show fungi in scrapings from the hands, but on one occasion Monilia albicans was recovered from the macerated skin between the toes.

For several months the patient used 20 per cent salicylic acid ointment, with little improvement. From June 27, 1936, to Feb. 19, 1937, she received twelve treatments of 75 r of unfiltered roentgen rays to the palm and dorsum of each hand. It was thought that some improvement had taken place after eight treatments, but after the twelfth treatment it was evident that no real change in her condition had occurred. Roentgen therapy was stopped and the patient was given two courses of solution of potassium arsenite and used an ointment containing salicylic acid from time to time, with no lasting beneficial effect. On June 15, 1937, her basal metabolic rate was + 2.5 per cent, and her palms and soles were in about the same condition as at the time of her first visit.

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29. This case was presented by Dr. J. Frank Fraser at a meeting of the New York Dermatological Society on Feb. 25, 1936 (Arch. Dermat. & Syph. **34**:1077 [Dec.] 1936) and by one of us (H. D. N.) at a meeting of the Section of Dermatology and Syphilis of the New York Academy of Medicine on Jan. 5, 1937 (ibid. **36**:887 [Oct.] 1937), and at a meeting of the Metropolitan Dermatological Society on April 19, 1937.

Fig. 1 (case 2).—Maceration, thickening, scaling and fissuring of the palms, extending to the flexures of the wrists.

Fig. 2 (case 2).—Hyperkeratosis, maceration and scaling of the soles.

CASE 3.[30]—F. S., a boy aged 8 years, born in the United States, was seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 28, 1936, because of an eruption on his palms and soles which had been present since birth. Both parents were born in the United States but

Fig. 3 (case 2).—Erythema, thickening and scaling of the dorsa and sides of the fingers.

Fig. 4 (Case 2.—Hyperkeratotic nodule on the internal malleolus and scaling, erythema and thickening of the skin on the side of the foot.

30. This case was presented by one of us (H. D. N.) before the Section of Dermatology and Syphilis of the New York Academy of Medicine on Dec. 1, 1936 (Arch. Dermat. & Syph. **36**:436 [Aug.] 1937).

both grandfathers were born in Italy. Neither his mother nor any maternal relative had any cutaneous abnormality, but his father, a paternal uncle, his grandfather and a granduncle had a similar hyperkeratotic condition of the palms and soles. None of the female members of his father's family nor the patient's younger sister had been affected. The patient's palms and soles were abnormal at birth, and the condition had not changed in the past five years.

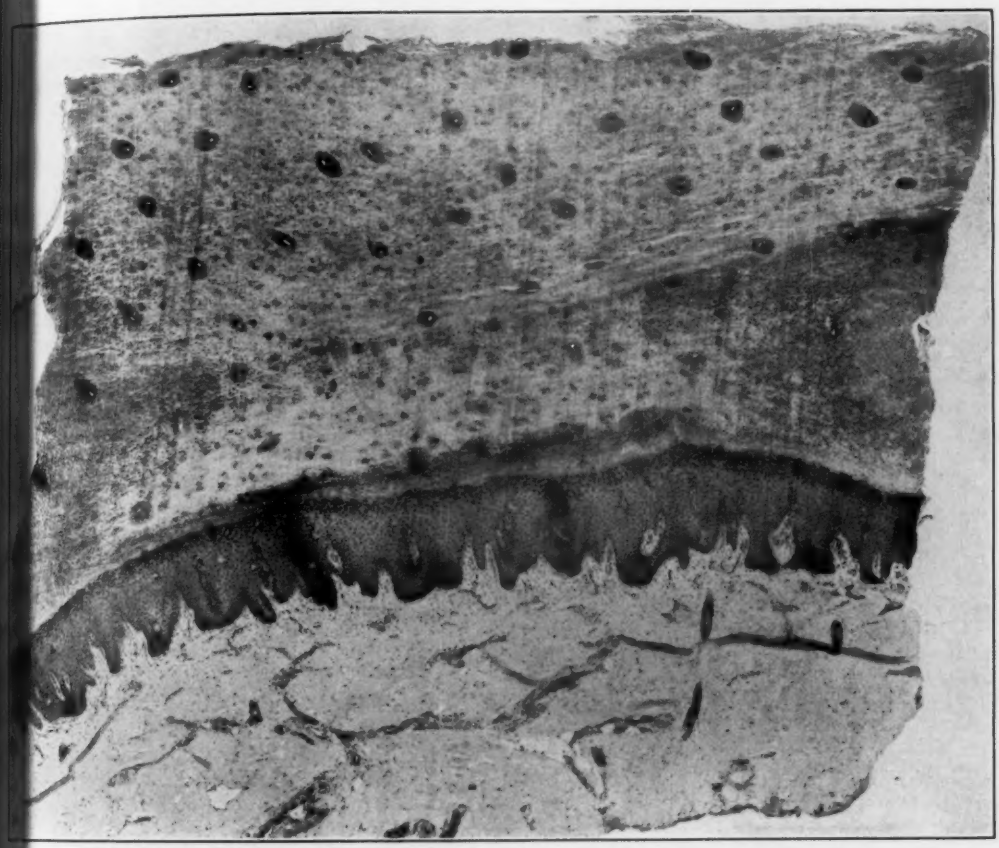

Fig. 5 (case 2).—Marked hyperkeratosis. The horny layer is more than twice as thick as the rest of the epidermis and cutis.

Examination showed the skin of both palms and soles to be waxy yellow, moist, greasy, hyperkeratotic, thickened and fissured. There were similar thickening and fissuring of the dorsal surface of the first interspace of each hand. The arrangement of the fissures between the hyperkeratotic areas on the soles produced a leaflike appearance. There was ichthyotic thickening of the skin over the knees and elbows and the dorsal and medial aspect of the ankles. The patient did not return for further observation.

CASE 4.[31]—C. M., a girl aged 1 year, was first seen by us on Aug. 10, 1937, at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, because of an involvement of the palms and soles of about nine months' duration.

The patient's mother was born in the United States, but her ancestors as well as the father and his ancestors came from Hungary. The parents were not related. The patient's father was a mechanic and had thickened palms, but they were not erythematous and there was no hyperhidrosis or odor. His soles showed no thickening. He attributed the condition of his hands to irritation from his work. No other members of the family had any cutaneous disease. When the patient was 3 months old, redness of the palms and soles appeared, and shortly after this a rancid fetid odor and excessive perspiration of the feet were first noticed.

Fig. 6 (case 4).—Erythema and thickening of the palms, extending to the flexures of the wrists.

Examination showed the skin of the palms (fig. 6) and soles to be diffusely erythematous and slightly moist and separated from the normal skin by a bluish red border about 0.5 cm. wide. This extended to the dorsa of the interspaces and the lateral surfaces of the fingers and toes, the flexures of the wrists, the sides of the soles and the achilles tendons. There was some hyperhidrosis and a definite rancid yeastlike odor on the palms and soles. The baby otherwise was in good health and had no other cutaneous lesions or abnormalities.

Salicylic acid ointments were applied, but they merely caused peeling, with no improvement in the condition. An ointment containing 5 per cent aluminum

31. This case was presented by one of us (H. D. N.) at the staff conference of the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, on Nov. 16, 1937.

Fig. 5 (case 2).—Marked hyperkeratosis. The horny layer is over twice as

chloride was then prescribed, in an attempt to lessen the objectionable odor, but this seemed to cause great dryness of the soles with subsequent fissuring and was abandoned. The patient was last seen on June 9, 1938, at which time the skin of the palms and soles was somewhat less red and thickened than on her previous visit.

SUMMARY

The chief features of mal de Meleda are reviewed.

Our reasons for considering mal de Meleda a special atypical form of, and not the same as, keratoma palmare et plantare hereditarium (Unna) are set out.

Four cases are reported. In 1 of these there was great improvement for more than two years following roentgen therapy.

114 East Fifty-Fourth Street.

BLENNORRHAGIC BALANITIFORM KERATODERMA

REPORT OF THREE ADDITIONAL CASES, INCLUDING ONE OF BUCCAL INVOLVEMENT

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In a recently published article [1] two of us discussed a case of penile blennorrhagic keratoderma of abortive course and of a clinical appearance so closely resembling balanitis sicca circinata that the true nature of the lesion was revealed only by microscopic examination. Similar findings in the literature induced us to believe that so-called balanitis circinata sicca gonorrhoeica is actually penile keratoderma. Such a conception will prove of great practical interest because, unlike balanitis, blennorrhagic keratoderma indicates systemic gonorrheal infection. Furthermore, keratoderma is part of a definite syndrome which includes arthritis that is nonankylosing, as well as endogenous conjunctivitis (Chauffard and Fiessinger [2]). Since our previous publication 3 additional cases have come under our observation. These form the basis of this report.

REPORT OF CASES

CASE 1.—E. H., a white man aged 31, first noticed a urethral discharge on Jan. 5, 1938. He received no treatment for three weeks. The appearance of a penile sore at that time induced him to consult a physician, who prescribed sulfanilamide. Some days later stiffness and pain in the neck developed, and he noticed several additional sores on the glans penis. On February 16 he entered the Dr. William J. Seymour Hospital because of an increased urethral discharge, tenderness and stiffness of the neck.

The patient was fairly well developed and appeared rather ill. His temperature showed slight elevation in the afternoon. There were mild conjunctivitis and increased lacrimation. A profuse purulent urethral discharge was present. The prostate was tender, enlarged and boggy. Smears of urethral and prostatic fluid contained many leukocytes and gram-negative intracellular gonococci. The glans

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From the Departments of Dermatology, Pathology and Urology, Dr. William J. Seymour Hospital.

1. Blumenthal, F., and Sherman, W. L.: Penile Blennorrhagic Keratoderma with Abortive Course, Am. J. Syph., Gonor. & Ven. Dis. **22**:176, 1938.

2. Chauffard, A., and Fiessinger, N.: Deux cas de keratose blenorrhagique, in Neisser, A., and Jacobi, E.: Ikonographia dermatologica, Berlin, Urban & Schwarzenberg, 1910, vol. 1, p. 193.

penis and prepuce were covered with round sharply bordered flat deep red papules about 0.5 cm. in diameter (fig. 1). There was no marked infiltration of the skin or tenderness on palpation. On removal of the adherent scales, a slightly moist surface was revealed, but no capillary bleeding was produced. Similar lesions were seen on the buccal mucosa. On both sides of the hard palate, directly above the margins of the gums, there were plaques of irregular size, with shallow centers, which were not tender on palpation (fig. 2). The individual lesions showed erythematous borders, the bases of which were grayish red. The mucosa of the pharynx and the tonsils, which were hypertrophic, showed marked injection. Because of tenderness and rigidity, the neck could be moved only with great difficulty and pain. The chest and abdomen showed nothing abnormal.

Fig. 1 (case 1).—Blennorrhagic balanitiform keratoderma.

An intradermal test with 0.1 cc. of gonococcus vaccine gave a strongly positive result after twenty-four hours, and the reaction remained for several days. Repeated dark field examinations of the penile lesions at twenty-four hour intervals showed no spirochetes. The Kahn and the Kline exclusion test were negative on February 18 and 28. On February 26 swelling, redness and tenderness appeared in the third right toe. Tenderness and rigidity of the neck still persisted. The pain and swelling of the neck and toe and the keratotic cutaneous and buccal lesions gradually subsided. On March 10 a roentgenogram of the cervical vertebrae showed no evidence of osseous or articular disease. On March 12 a roentgenogram of the right foot and ankle showed spur formation between the upper posterior portion and the margin of the scaphoid bone and the upper anterior margin of the astragalus. The spur on the scaphoid bone appeared to have resulted from an old fracture. There were no findings suggestive of arthritis.

The patient was treated with sulfanilamide, by diathermy and by intramuscular injection of sterile milk. On April 22 the patient was still in the hospital com-

plaining of tenderness in the right foot and ankle, but there was no redness or swelling in the joints, and the neck could be moved without pain. The cutaneous and buccal eruptions had completely disappeared. There was no urethral discharge; the prostate was of normal size and not tender, and smears of the prostatic fluid were normal.

Fig 2 (case 1).—Lesion of the hard palate.

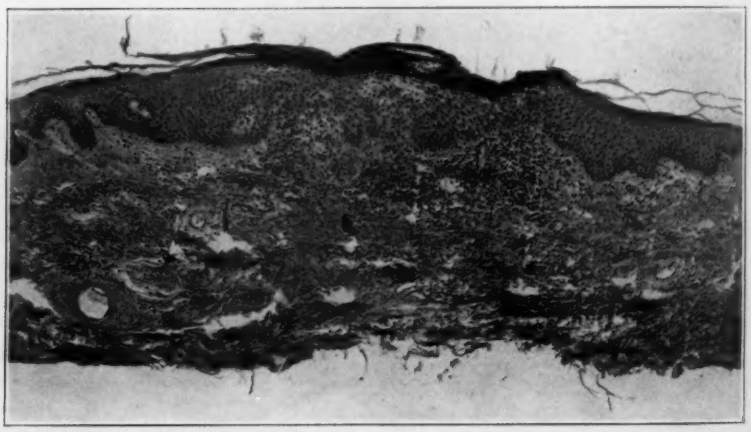

Fig. 3 (case 1).—Microscopic picture of blennorrhagic balanitiform keratoderma.

Microscopic examination of cutaneous lesions of the prepuce showed "elevation of the epidermis due to some intracellular and much intercellular edema of the upper strata of the rete and edema so marked as to cause the formation of small intercellular spaces filled with fluid and leukocytes. The surface was covered by a crust of parakeratotic lamellae and leukocytes, the upper layers of which

were continuous with the surrounding normal keratin. The lower strata of the rete Malpighii showed slight hypertrophy and an increase in the number of mitotic figures at the borders of the lesions. There were degenerative changes due to marked edema of the corium in the center of the lesions, which contanied numerous capillaries with swollen endothelium and a moderately dense cellular infiltration composed of lymphocytes, polymorphonuclear leukocytes and plasma cells. The diagnosis was early lesion of keratoderma gonorrhoeicum" (fig. 3).

Microscopic examination of a mucosal lesion taken from the roof of the mouth showed leukokeratotic changes. There was a zone of marked edema of the papillae and the upper part of the epithelium. There were spongiosis and cleft formation in the superficial parts of the rete. There was transmigration of leukocytes, but only slight cellular infiltration of the papillary body.

CASE 2.—J. L., a white man aged 20, in November 1937 noticed a urethral discharge, which disappeared after one week of self treatment. On Jan. 5, 1938,

Fig. 4 (case 2).—Blennorrhagic balanitiform keratoderma.

after a drinking bout, the discharge reappeared, and on the afternoon of the same day the left ankle and some of the right toes became painful. On Jan. 6, 1938, he was admitted to the Dr. William J. Seymour Hospital, complaining of burning on urination, a profuse urethral discharge and exquisite tenderness and marked swelling of the left ankle and some of the right toes. The patient was rather well developed and did not appear acutely ill. There was a profuse purulent urethral discharge. The prostate was slightly tender, enlarged and boggy. Smears of the urethral and prostatic fluid contained many leukocytes and intracellular gram-negative diplococci. The left ankle and the right second, third and fourth toes were tender, swollen and red. The chest and the abdomen were normal. The Kahn and the Kline exclusion test were negative. The temperature was normal. The patient was treated with sulfanilamide and by hyperpyrexia. Four weeks later, scaling reddish penile lesions appeared (fig. 4). On February 26 the greater part of the glans and the prepuce were involved. While the early

lesions appeared vesicular, the older ones were papules ranging in size from that of a pin to that of a pea and covered by a brownish yellow crust, which coalesced and appeared circinate. On removal of the scales, a red slightly oozing flat surface was revealed. The eyes showed only increased lacrimation. On March 2 a roentgenogram showed no evidence of osseous or articular change.

Under treatment the cutaneous lesions disappeared; there was no urethral discharge, and the articular symptoms subsided. A smear of the prostatic fluid demonstrated many leukocytes but no gonococci. The intradermal reaction to gonococcus vaccine was strongly positive after twenty-four hours and persisted for some days in the same strength. The patient was discharged on March 13, 1938.

Microscopic examination of a cutaneous penile lesion showed the epidermis to be slightly acanthotic in places and the rete pegs plump. There was spotty intercellular edema of the suprapapillary layers, with transmigration of some leuko-

Fig. 5 (case 3).—Blennorrhagic balanitiform keratoderma.

cytes. The surface was covered by a scale of compressed parakeratotic layers, between which there was an occasional accumulation of pyknotic leukocytes. In some areas the parakeratotic layers were separated from the rete Malpighii by a thin fiber of normal keratin and keratohyaline cells. The papillae were moderately edematous, with prominent endothelium of the capillaries. The subpapillary layers contained rather diffuse infiltration of lymphocytes and a few plasma cells. A diagnosis of keratoderma gonorrhoeicum in the dry, chronic stage was made.

Case 3.—W. R., a white man aged 25, first noticed a urethral discharge on March 27, 1938; some vague pains in the back began three days later, and there was suprapubic itching. He was admitted to the Dr. William J. Seymour Hospital on April 5, with an abundant purulent urethral discharge, some backache and continued suprapubic itching. Examination revealed him to be well developed and not acutely ill, with some stiffness in his back on motion, marked excoriation of

the suprapubic area, where pediculi pubis were found, and an abundant urethal discharge showing gram-negative intracellular diplococci. The patient was treated with large doses of sulfanilamide. A few days later the temperature became elevated, and he suffered a gastric upset and increased tenderness and stiffness of the back. Sulfanilamide was discontinued. The gastric disturbance and fever disappeared, but the pains in the back and a slight urethral discharge continued. On April 17 a small round sharply bordered deep red flat papule (fig. 5) appeared on the glans penis and was soon covered with an adherent scale. Several days later the lesions were abundant, extending from the glans onto the prepuce on the dorsal surface and coalescing to give a circinate appearance. There was no capillary bleeding or secretion of lymph. Typhoid vaccine therapy was given after the upset. An intradermal test with 0.1 cc. of gonococcus vaccine gave a strongly positive reaction. The eyes showed increased lacrimation. On April 19 smears of the urethral and prostatic fluid showed no organisms. The prostate was of normal size, shape and consistency. By April 30 all signs and symptoms had disappeared, and the patient was ready for discharge. Material for biopsy could not be secured.

Comment.—These 3 cases manifest the characteristics of penile abortive keratoderma blennorrhagicum outlined in our previous paper. Cutaneous dyskeratotic lesions and arthritis appeared simultaneously during an exacerbation of urethritis and prostatitis, along with mild conjunctivitis with increased lacrimation of both eyes. Gonococci were found in smears of urethral and prostatic fluid, but were absent in both the cutaneous lesions and the blood stream. The intradermal reaction was strongly positive. All patients complained chiefly of arthritic pains, in the neck and third right toe in the first case, in the right ankle and several right toes in the second and in the spine in the third. There were tenderness, redness and swelling, but no effusion or tendency to ankylosis, commonly seen in gonorrheal monarthritis.

The cutaneous eruptions were confined chiefly to the penis; the single papules were round and sharply bordered and coalesced to form circinate plaques. After removal of the yellow-reddish crumbling crust, a flat, slightly moist surface appeared. In case 2 the lesions were darker and larger but not fundamentally different from those in the others and reminded us of balanitis erosiva, while those in the first and the third case resembled balanitis sicca.

Syphilis must be considered first in the differential diagnosis and psoriasis and herpes progenitalis next. There are no infiltration or abundant secretion of lymph, as in syphilis, no capillary bleeding, as in psoriasis, and no tenderness or polycyclic configuration, as in herpes progenitalis.

The finding of keratotic lesions involving the mucous membrane of the hard palate was highly surprising, because such an incident even in generalized keratoderma is rare. The anatomic studies were of major interest. Previously we had the opportunity of studying only a fully developed papule. However, this time we were fortunate in getting

specimens showing different stages of development. In case 1 the lesion was very early, and in case 2 the biopsy specimen was taken from a subsiding papule. Even in these specimens there was evidence of all the characteristic changes to be expected in keratoderma. In case 1 there was intracellular and particularly intercellular edema of the upper part of the rete. This edema produced small intercellular spaces, which were filled with fluid and leukocytes. The upper layer of the surface was covered with a parakeratotic crust and leukocytes, but was still surrounded by normal keratin. Obviously the lesion was in a still earlier stage than that seen by Keim,[3] who described a vesicle as the earliest lesion. In the second case the intercellular edema was more spotty, and in some places the parakeratotic layers were separated from the rete by a thin fiber of normal keratin and keratohyalin, showing that we were dealing with a stage of regeneration of the cutis. The presence of dense infiltration with numerous plasma cells occupying the upper part of the cutis may be emphasized. This constant finding is of special interest, being the most important anatomic argument, as was pointed out by Stryker and Ham,[4] against the identity of keratoderma and arthropathic psoriasis.

In our previous publication we expressed the belief that blennorrhagic keratoderma is not as rare as it would appear; in fact, among 240 gonorrheal patients treated in the Dr. William J. Seymour Hospital during the last eighteen months, there were 4 with balanitiform keratoderma, a frequency exceeding that reported by Arning and Meyer-Delius (0.5 per cent).[5] However, our greater frequency might have been expected from the fact that we were dealing mostly with hospitalized patients and, therefore, with patients with a relatively high incidence of arthritic involvement.

As explained in our previous paper, blennorrhagic keratoderma must be considered a microbid.[6] In fact, this condition shows all the characteristics of a toxoallergic reaction. There are peculiar endogenous cutaneous manifestations differing from true septicemic eruptions and depending in their course on the progress of the primary focus. There are conjunctivitis and arthritis of an allergic type with a strongly positive intradermal reaction. Gonococci are not found in the meta-

3. Keim, H. L.: The Histogenesis of Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **9**:423 (April) 1924.

4. Stryker, G. V., and Ham, A. W.: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **26**:684 (Oct.) 1932.

5. Arning, E., and Meyer-Delius, H.: Beitrag zur Klinik gonorrhoischen Hyperkeratosen, Arch. f. Dermat. u. Syph. **108**:13, 1911.

6. Oliver S. Ormsby, in discussing a case presented by M. H. Ebert and A. Slepyan before the Chicago Dermatological Society (A Case for Diagnosis [Keratosis Blennorrhagica?], Arch. Dermat. & Syph. **37**:106 [Jan.] 1938), expressed a similar opinion.

static lesions. Therefore, the condition represents the combined effect of gonococci and of an allergic body reaction causing a rapid split of the microbe.

Such considerations are of great practical interest and will influence our therapy in many ways. It is obvious that eruptions of this type will be of diagnostic help, in that they justify assumption of a still active infectious focus. The simultaneous presence of balanitiform keratoderma and arthritis will therefore point to a toxoallergic form of gonorrheal articular involvement, for, although in gonorrhea the history and the course of the disease sufficiently clarify the condition, doubt as to the nature of the articular changes not infrequently arises.

For treatment, and at the same time as a preventive measure, the principal task will be to eradicate the primary focus. Local treatment of the joints and of the cutaneous lesions is of only secondary value. In fact, arthritis, as well as the lesions of the mucous membrane, disappears when the primary focus is treated.

SUMMARY AND CONCLUSIONS

Three additional cases of balanitiform blennorrhagic keratoderma with abortive course are described, in 1 of which there were mucosal lesions of the hard palate.

Balanitiform keratoderma points exclusively to an infectious gonorrheal background.

Balanitiform keratoderma together with arthritis and endogenous conjunctivitis is part of a special syndrome due to a toxoallergic mechanism similar to that seen in tuberculid and other microbids.

Microscopic examination of early lesions showed formation of a cleft in an area of intercellular edema, which will lead to a vesicle. The cutis was infiltrated with numerous plasma cells, a point of contrast to the otherwise similar picture of psoriasis vulgaris.

Treatment of the primary focus is of main importance, local treatment of the cutaneous and arthritic condition being only of secondary value.

ONYCHODYSTROPHY CAUSED BY CERVICAL RIB

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AND
ANTHONY C. CIPOLLARO, M.D.
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Weidman [1] has recently called attention to dermatoses affecting one hand, resulting from the presence of cervical rib. He mentioned 2 cases which he observed personally, 1 of congenital trophic ulcer of one finger in a child of 6 years and 1 of peculiar dermatitis of one hand in an adult. A review of the literature revealed only 5 reports of cutaneous changes ascribed to the presence of cervical rib. Gaté, Thiers and Racouchot [2] reported the case of a peasant, aged 50, who had an eczematous eruption of both hands, but more severe on the right palm, with atrophy of the bones of the right hand. The nails of both hands were grooved. A roentgenogram of the cervical segment of the spine showed a cervical rib on the right. Holthaus [3] described a case of cervical rib on the right, with vasomotor disturbance producing dry gangrene of the tip of the third right finger, and cyanosis of the tips of the second, fourth and fifth right fingers. Perrot [4] mentioned the following trophic and vasomotor disturbances due to cervical rib: glossy skin of the terminal phalanges, changes in the nails, ulceration of the fingers, peripheral vasoconstriction, chronic edema with cyanosis and Raynaud's syndrome. Craig and Knepper [5] called attention to the fact that unilateral or bilateral rudimentary cervical ribs may cause pain in the neck, arm or hand and circulatory and trophic changes in the upper extremities. These changes are manifested as pain, numbness, cyanosis, atrophy, ulcers or even gangrene. Hyperesthesia, paresthesia or anesthesia may be present.

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University.

1. Weidman, F. D.: Cervical Ribs (?), Arch. Dermat. & Syph. **35**:716 (April) 1937.

2. Gaté, J.; Thiers, H., and Racouchot, J.: Syndrome sympathique des régions palmaires, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Lyon) **44**:730 (June) 1937.

3. Holthaus, B.: Ueber nervöse Folgezustände von Halsrippen, Deutsche Ztschr. f. Nervenh. **114**:114, 1930.

4. Perrot, A.: Côtes cervicales: Une complication rare, Schweiz. med. Wchnschr. **64**:559 (June 16) 1934.

5. Craig, W. M., and Knepper, P. A.: Cervical Rib and Scalenus Anticus Syndrome, Ann. Surg. **105**:556 (April) 1937.

Many articles dealing with various surgical and medical conditions caused by cervical ribs have been written. Putti [6] reported a case of right cervical rib associated with aneurysm of the right subclavian artery in which ulceration of the right index finger, edema, cyanosis, changes in temperature, paresthesia of the hand and paleness of the finger nails were present.

Cervical rib does not always cause symptoms. The appearance of unusual unilateral dermatoses of the upper extremities should make one suspect the presence of this abnormality and calls for a roentgenogram of the cervical segment of the spine. Cervical rib is a congenital anomaly, but symptoms usually do not develop until after the second or third decade.

Craig and Knepper [5] have carefully studied the mechanism by which cervical rib causes circulatory and trophic changes. The cutaneous changes are caused by pressure on the subclavian vessels or on the

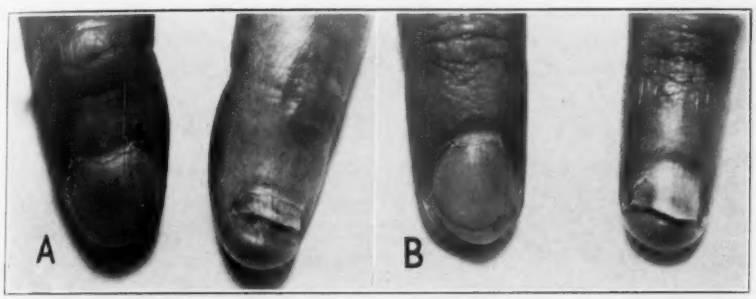

Fig. 1.—*A*, comparison of the normal right thumb with the involved left thumb. The left thumb is smaller and shows dystrophy of the nail and atrophy of the skin. *B*, comparison of the normal right middle finger with the involved left middle finger. The left finger is smaller and shows dystrophy of the nail and atrophy of the skin.

brachial plexus. The scalenus anticus muscle, which arises from the anterior tubercles of the transverse processes of the third to the sixth cervical vertebrae and is inserted into the scalene tubercle of the first rib, compresses these structures against the cervical rib. The cervical rib may compress and irritate the brachial plexus, thus causing spasm of the scalenus anticus muscle, which is innervated by a twig from the plexus. A spasm of the scalenus anticus muscle may elevate the first rib and so cause the compression of the subclavian vessels and brachial plexus. Elevation of the chin or rotation of the head toward the affected side on inspiration may temporarily obliterate the radial pulse in such cases.

6. Putti, V.: Costola cervicale e aneurisma della succlavia, Boll. e mem. d. Soc. Emiliano-Romagnola di chir. **2**:138 (Feb.) 1936.

Fig. 2.—Roentgenograms of hands, showing atrophy and absorption of lime salts in the terminal tufts of the left thumb and middle finger. (*L* denotes left hand).

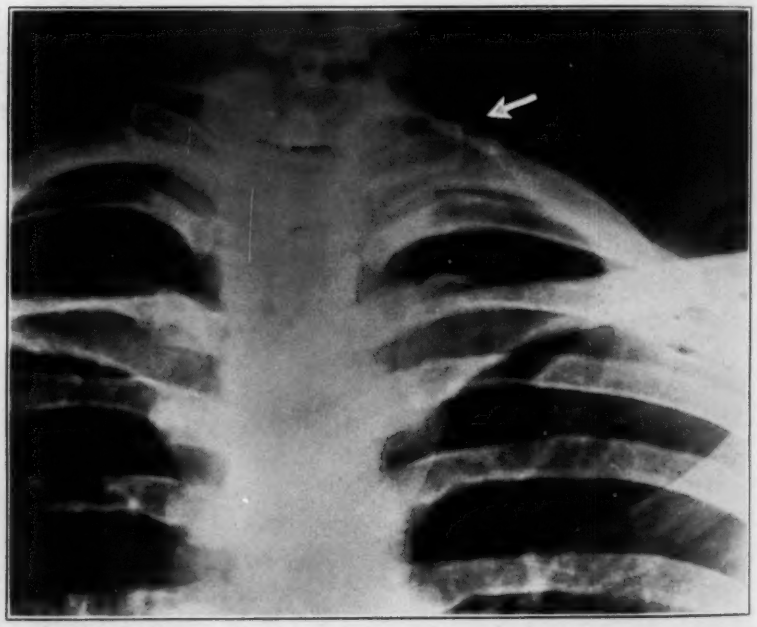

Fig. 3.—Roentgenogram showing articulated cervical rib on the left side (arrow). There is no cervical rib on the right side.

We wish to report a case in which changes in the nails, the terminal carpal bones and the overlying skin were the presenting symptoms.

REPORT OF CASE [7]

L. S., a Jewess aged 25, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complaining of ungual changes of two years' duration. The family and past history were irrelevant. General physical examination showed no abnormality. Local examination showed the terminal phalanges of the left thumb and middle finger to be involved. The nails were opaque, yellowish, ridged and shortened. The free or distal edges were everted and raised from the nail bed. There was no subungual hyperkeratosis or pitting. The skin of the two terminal phalanges was shiny, whitish, thin and atrophic. The phalanges themselves were smaller than normal and tapering. There was no pain, anesthesia or hyperesthesia. Ulceration was not present. The paronychial tissues showed no inflammation. There was no clinical or laboratory evidence of dermatophytosis or psoriasis locally or elsewhere on the body. The toe nails and the other eight nails of the hands were normal. The radial pulses were equal, regular and synchronous. On marked extension of the head the radial pulse on the left side was momentarily obliterated.

Laboratory Findings.—The Wassermann and the Kahn test were negative. The basal metabolic rate was within normal limits. Chemical analysis of the blood showed 11.5 mg. of calcium and 2.1 mg. of phosphorus per hundred cubic centimeters. Scales and clippings of the nails showed no fungi on repeated examination and culture. Roentgenograms of both hands, read by Dr. William Meyer showed a moderate degree of absorption of lime salts more or less throughout the bones of the left hand. The atrophic condition was a shade more discernible in the terminal tufts of the thumb and middle finger. A roentgenogram of the cervical portion of the spine showed an articulated cervical rib on the left side of the seventh cervical vertebra; this articulated portion extended downward and forward about 1 inch (2.5 cm.) and tapered toward the distal end.

SUMMARY

Attention is called to the fact that some unilateral conditions of the skin of the upper extremities may be caused by pressure phenomena associated with the presence of cervical rib. The literature is reviewed, and 1 new case is reported.

Drs. G. M. MacKee and Isadore Rosen permitted us to publish this report.

5 East Fifty-Third Street.

40 East Sixty-First Street.

7. This case was presented before the Manhattan Dermatologic Society on Oct. 12, 1937 (Arch. Dermat. & Syph. **37**:530 [March] 1938), and again on Jan. 11, 1938 (ibid. **37**:917 [May] 1938), by Dr. Cipollaro.

KERION CELSI OF THE SCALP IN AN ADULT

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It is well recognized that ringworm of the adult scalp, especially the kerionic type, is rare in all parts of the civilized world and especially so in the United States. Fox and Fowlkes [1] pointed out this fact in 1925, tabulating 50 proved cases from the world literature, of which 4 were reported in the American literature. To this series they added 3 cases of their own. They found the kerionic type in 7 instances, including their own case. Since that time a relatively larger number of cases have been reported in the foreign literature, but the scarcity of reports of the condition in the United States is noteworthy.

Fox [2] added another case of ringworm of the adult scalp in 1926. Additional reports in the American literature have been made by Chambers,[3] Bechet,[4] Andrews,[5] White [6] and Cummer,[7] making a total of 15 cases in which the diagnosis was proved by microscopic or cultural examination.

The rarity of ringworm of the adult scalp in the United States is in contrast with the findings of investigators in foreign lands, especially in Europe and the Orient, where representative reports indicate a much higher incidence. Maschkilleisson [8] in 1936 collected 606 cases mentioned in the literature, with detailed reports of 466. No mention was made of verification of the diagnosis by culture or by microscopic examination,

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From the University of Michigan Medical School, service of Dr. Udo J. Wile.

1. Fox, H., and Fowlkes, R.: Ringworm of the Scalp in Adults, Arch. Dermat. & Syph. **11**:446 (April) 1925.

2. Fox, H.: Ringworm of the Scalp in an Adult, Arch. Dermat. & Syph. **13**: 398 (March) 1926.

3. Chambers, S. O.: Ringworm of the Scalp Occurring in an Adult, Arch. Dermat. & Syph. **13**:447 (March) 1926.

4. Bechet, P. E.: Tinea Tonsurans in an Adult, Arch. Dermat. & Syph. **13**: 710 (May) 1926.

5. Andrews, G. C.: Kerion Celsi: Lichen Trichophyticus, Arch. Dermat. & Syph. **16**:477 (Oct.) 1927.

6. White, C.: Ringworm of the Scalp in Adults, Illinois M. J. **56**:152 (Aug.) 1929.

7. Cummer, C. L.: Tinea Capitis with Kerion in an Adult, Arch. Dermat. & Syph. **36**:844 (Oct.) 1927.

8. Maschkilleisson, L. N.: Zur Frage über Trychophytia superficialis capillitii adultorum, Dermat. Wchnschr. **102**:765 (June 13) 1936.

but from his clinic a series of 54 cases was collected during the period 1927 to 1935, in 24 of which the diagnosis was proved by culture and the organism identified. Another series of 21 cases was reported by Chen and Kurotchkin[9] from China, in all of which the condition was identified grossly, microscopically and by culture. This large series was collected during a two year period at the clinic of the Union Medical College in Peiping, China, the authors expressing the opinion that the disease is much more common in China than it has been reported to be in other parts of the world.

Because of the rarity of ringworm of the adult scalp in the United States, and especially the kerionic type, the following case is reported:

REPORT OF A CASE

M. M., a Negress aged 51, single, was admitted to the University Hospital Jan. 14, 1938, for treatment of a lesion of the scalp. She had first noticed the lesion, a week previously, as a slight swelling accompanied by mild pruritus. During the following three or four days the lesion enlarged and became tender, and pus exuded from separate points. The patient noticed also that the hairs were falling out in this area and that some were broken off close to the surface of the scalp. There was no history of a previous lesion of the scalp or of any eruption on the extremities or the trunk. The patient had been employed for a number of years as a maid in a ward for adult patients in this hospital, and there had been no contact with children or domestic animals. She stated, however, that she had made periodic visits to a hairdressing establishment where children were also patrons.

General examination revealed no eruption of the glabrous skin. The lesion of the scalp consisted of a circumscribed tumescence 7 by 5 by 1.5 cm., located just to the left of the midline, overlying the medioposterior portion of the parietal bone on the left (fig. 1). The surface of the tumor was irregular, and most of the scalp hair was missing. The few remaining hairs were broken off close to the surface and could be removed easily with gentle traction. About and between these groups of hair stumps was seen grayish rounded elevations ranging in size from that of the head of a glass pin to that of a grain of wheat. They were distended with gray-yellow pus and ruptured rather easily on gentle pressure. When the pus was expressed, a ragged, shallow crater remained, the base and walls being pinkish gray and bleeding easily. The periphery of the tumor rose sharply from the normal scalp surrounding it and was of the same character as the central portion of the lesion, the general impression on palpation being that of a boggy or doughy consistency. Pain was elicited only on deep pressure. Just lateral to the lesion and separated by 4 cm. of normal scalp were two penny-sized, slightly elevated scaly patches which resembled the lesions of superficial ringworm of the scalp. The causative organism was also isolated in cultures of material from these areas.

Microscopic examination of the hairs revealed spores arranged in a mosaic pattern and a few fine hyphae in a few preparations. Material from the lesion was planted on Sabouraud's agar, and in eight days a small whitish colony was

9. Chen, F. K., and Kurotchkin, T. J.: Tinea of Scalp Among Adults in Peiping, Nat. M. J. China **17**:185 (April) 1931.

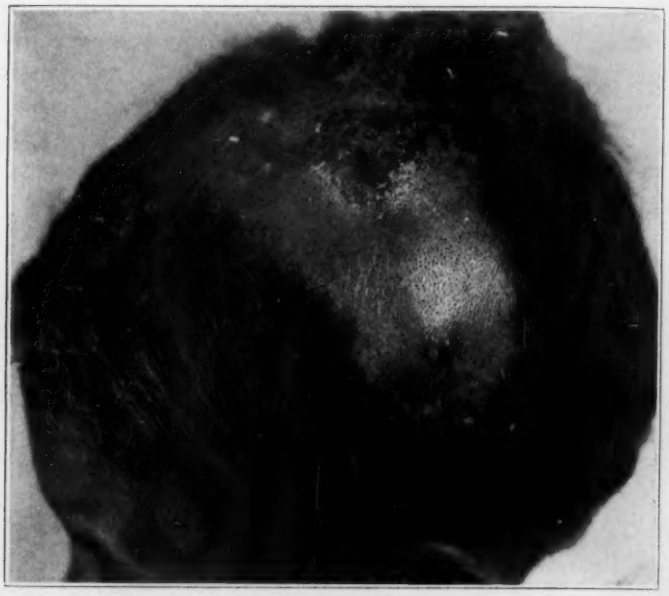

Fig. 1.—Kerion of the scalp in an adult.

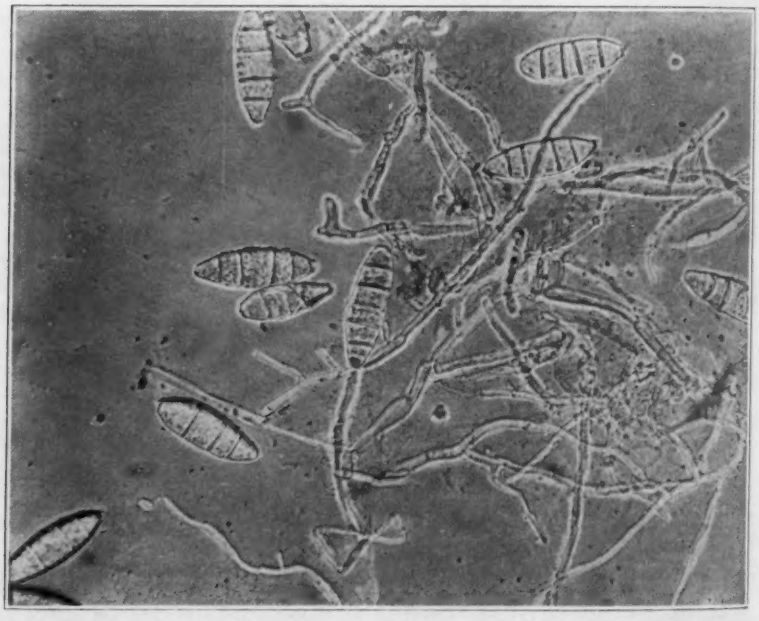

Fig. 2.—Eight day old culture on Sabouraud's medium, showing the mycelial network, with production of raquette cells, young conidiophores and large septate macroconidia.

visible. Growth was fairly rapid, the periphery extending in a radiating lacelike network and the central substratum gradually assuming a cinnamon buff color. Microscopic examination of the young cultures showed a profuse mycelial growth with the production of numerous microconidia and large fusiform septate macroconidia, the surface of which was studded with warty outgrowths (fig. 2). Young conidiophores and so-called raquette cells or raquette hyphae were numerous. The gross and microscopic appearances were typical of Microsporon lanosum.

Treatment consisted of shaving of the surrounding area, manual epilation of the affected hairs, topical application of mild parasiticides and superficial roentgen therapy. The clinical course was uneventful, and complete involution of all lesions took place in approximately three weeks.

COMMENT

This is the fourth case to be reported in the American literature of kerion of the adult scalp and the sixteenth of either the kerionic or the superficial type of ringworm in which the diagnosis was proved by culture or microscopic examination. Ringworm of the adult scalp has occurred in Negroes in 7 instances, being of the kerionic type in 4. Ringworm of the adult scalp is rarely reported in the American literature but is relatively common in Europe and the Orient.

SUMMARY

An occurrence of kerion Celsi in an adult Negress is reported. Microsporon lanosum was identified by gross and microscopic examination.

CRITERIA FOR THE HISTOLOGIC DIAGNOSIS OF KERATOSIS FOLLICULARIS (DARIER)

REPORT OF A CASE WITH VESICULATION

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This report of a case of Darier's disease was prompted by the unusual moisture and vesiculation, which were prominent features, and particularly by the confusion of the diagnosis with possible pemphigus vegetans. We wish to stress that the histologic features of Darier's disease are fairly clearcut, that the presence of moisture and crusting has hitherto not been emphasized and that vesiculation may be prominent to a degree which may obscure correct diagnosis. A brief summary of the reports of moist lesions in this rare condition and some comments on its pathogenesis are also in order.

The patient was exhibited at the clinic of the dermatologic section of the Southern Medical Association in November 1936, and the evidence presented for the diagnosis of Darier's disease was generally accepted.

The first case of this disease was reported by White,[1] and the pathologic changes were described by J. T. Bowen. There were three characteristic clinical features: hyperkeratosis, follicular location and crusting. Darier's report of his first case [2] appeared within the following two months, and he frankly accepted White's case as belonging to the same group. He quoted from Thibault,[3] to include 2 additional examples.

From the Department of Dermatology of the Johns Hopkins School of Medicine and Hospital.

Read at the Sixty-First Annual Meeting of the American Dermatological Association, Inc., Del Monte, Calif., June 10, 1938.

1. White, J. C.: A Case of Keratosis (Ichthyosis) Follicularis, J. Cutan. & Genito-Urin. Dis. **7**:201 (June) 1889.

2. Darier, J.: Psorospermose folliculaire végétante, Ann. de dermat. et syph. **10**:597 (July) 1889.

3. Thibault, A.: Observations cliniques pour servir à l'histoire de la psorospermose folliculaire végétante de Darier, affection cutanée non décrite, on comprise dans les groupes des acnés sébacées, cornées, hypertrophiantes, etc., Thesis, Paris, no. 214, Paris, G. Steinheil, 1889.

About two years previously Morrow [4] had published a case of "keratosis follicularis" with the histologic description by Robinson, but no mention was made of dyskeratotic changes in the rete mucosum.

It would be irrelevant to record the various microscopic pictures in these several cases, but they formed the foundation of the epidermal changes which are of interest today in the diagnostic evaluation of this unique disease.

The many reports elaborating the presence of *corps ronds* and grains in the dyskeratotic changes have been summarized and commented on in the excellent monograph of Brünauer.[5] Darier,[6] as is well known, in a second publication clarified his concept of the pathologic anatomy of the disease and relinquished the hitherto interesting concept of psorospermosis. The various titles proposed for this dermatosis need not claim attention here. We wish especially to direct attention to the presence of crusting; to the clinical observation of vesiculation on areas not intertriginous or subject to chafing, and, in microscopic sections, to the formation of lacunar or fissured areas in the rete.

The lesions have usually been considered to be dry, on account of the pronounced keratotic changes. Excepting the presence of the disease in seborrheic persons and in intertriginous areas where moisture is conducive to secondary infection and erosion—thus giving rise to the offensive odors so frequently described—we would rather stress the constant presence in certain patients of crusts and of eroded and frankly moist areas, which is entitled to more attention than it has hitherto received.

Since numerous reports deal with variants from the original description, and since the eruption may vary from dry, warty-appearing efflorescences to heavily crusted and actually vegetating lesions with or without impetiginous or simple vesicular changes, it is well to consider some possible factors in such appearances.

For example, a seborrheic background, the implantation of impetigo of various types and what some authors today consider to be the syndrome of eczema, deserve attention. Just what such complications, if they may be so termed, may do to effect a bizarre or unfamiliar picture in keratosis follicularis is speculative.

Though numerous reporters have stressed the dry, warty appearance of the eruption, many authors of textbooks have described the eruption as associated with moisture, even in the earliest stages.

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4. Morrow, P.: Keratosis Follicularis Associated with Fissuring of the Tongue and Leukoplakia Buccalis, J. Cutan. & Ven. Dis. **4**:257 (Sept.) 1886.

5. Brünauer, S. R.: Morbus Darier, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2, p. 210.

6. Darier, J.: Note sur l'anatomie pathologique de la maladie dite "Psorospermose folliculaire végétante" à propos d'un cas nouveau, Ann. de dermat. et syph. **7**:742, 1896.

Stelwagon [7] mentioned distinct fissuring, as well as moist openings, when secondary lesions were removed.

Jarisch [8] stated that on the underlying skin a red weeping spot often appeared, with small, funnel-like openings.

Crocker [9] wrote of papules having brown, black or gray horny crusts (moisture?).

Ormsby [10] viewed the lesions as "papules which soon become crust covered."

Pusey [11] wrote that in the "dilated follicular openings there may be infection with ulceration and purulent discharge."

Sutton [12] stated: "The primary lesions are partially covered by firmly adherent brownish or blackish, greasy horny crusts."

Macleod [13] described the lesions as "characterized by dirty brownish papules, covered with a horny crust, which tend to form crusted patches. . . . The crust when removed leaves a red weeping surface which may bleed."

Riecke [14] may be quoted: "The larger papules are covered mostly with dirty brown or yellowish gray scaly crusts and horny crusts; if these are removed there appear very flat prominences . . . sometimes with serous moisture."

Andrews [15] described the lesions as soon becoming "covered with a greasy, gray, brown or black crust."

Darier [16] considered the disease clinically as "papulocrusts, often follicular." "The typical eruptive lesion is a papule covered with a grayish brown crust."

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7. Stelwagon, H. W.: Treatise on Diseases of the Skin, for the Use of Advanced Students and Practitioners, ed. 6, Philadelphia, W. B. Saunders Company, 1910, p. 526.

8. Jarisch, A.: Die Hautkrankheiten, ed. 2, Vienna, A. Hölder, 1908, p. 690.

9. Crocker, H. R.: Diseases of the Skin: Their Description, Pathology, Diagnosis, and Treatment, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1910, p. 604.

10. Ormsby, O. S.: A Practical Treatise on Diseases of the Skin, for the Use of Students and Practitioners, Philadelphia, Lea & Febiger, 1915, p. 486.

11. Pusey, W. A.: The Principles and Practice of Dermatology, ed. 3, New York, D. Appleton and Company, 1917, p. 901.

12. Sutton, R. L.: Diseases of the Skin, ed. 6, St. Louis, C. V. Mosby Company, 1926, p. 490.

13. Macleod, J. M. H.: Diseases of the Skin: A Text-Book for Students and Practitioners, New York, Paul B. Hoeber, 1921, p. 1103.

14. Riecke, E.: Lehrbuch der Haut- und Geschlechtskrankheiten, ed. 7, Jena, Gustav Fischer, 1923, pp. 459-461.

15. Andrews, G. C.: Diseases of the Skin: A Text-Book for Practitioners and Students, Philadelphia, W. B. Saunders Company, 1930, p. 886.

16. Darier, J. A.: A Text-Book of Dermatology, edited by S. Pollitzer, Philadelphia, Lea & Febiger, 1920, p. 231.

These authors apparently inferred the initial production of moisture, if not frank vesiculation. We have cited these descriptions to substantiate, if possible, our belief that the primary changes in Darier's disease include the production, or the presence, of moisture or vesiculation. The histologic picture must speak for itself.

A number of rare dermatoses, such as Paget's dyskeratosis, certain types of epithelioma, molluscum contagiosum, unusual types of papilloma and verrucae and Bowen's dermatosis, reveal elements of dyskeratosis, including *corps ronds,* grains, clumped cells, giant epidermal cells and mitoses. In such diseases edema within the epidermis, if it should occur, is apparently incidental.

As our case revealed elements of both moisture and actual vesiculation, as well as some characteristic changes, it is pertinent to refer briefly to the available literature bearing on this aspect of the histologic picture.

Darier in his original description apparently did not consider the lacunar spaces and the fissuring to be of importance, and Brünauer mentioned these features as evidently of secondary consequence.

Apparently Boeck [17] was the first to observe and study seriously this lacunar formation, although Darier [6] in his second paper stressed this quality ("la désagrégation du corps muqueux est . . . frappante"). He further stated: "The primordial modification consists in degeneration, granular disintegration . . . even liquefaction of a certain number of cells of the mucous layer above the cylindric layer." This was an explanation of the origin of *corps ronds,* etc., rather than a discussion of the reason for the separation of the suprabasal layer into lacunas and fissures.

Boeck expressed the belief that the lacunar formation is the result of a loss of cohesion of the prickles, which permits the formation of spaces into which fluid may enter; and he reconciled these changes with the clinical lesions. Thus, vesicles and bullae were evidently exaggerations of microscopic lacunas.

Darier stated that "other cells of the mucous layer were disarranged by rupture of the filaments of union," and this even at the level of the interpapillary processes.

Pawloff,[18] Melle [19] and Bukovsky [20] reported cases in which moisture, vesiculation and maceration appeared to be complications rather

17. Boeck, C.: Vier Fälle von Darierscher Krankheit, Arch. f. Dermat. u. Syph. **23**:857, 1891.

18. Pawloff, T. P.: Zur Frage der sogenannten Psorospermose folliculaire végétante Darier, Arch. f. Dermat. u. Syph. **25**:195, 1893.

19. Melle, G.: Klinischer und anatomisch pathologischer Beitrag zum Studium der Psorospermosis cutanea vegetans, Monatsh. f. prakt. Dermat. **28**:143, 1899.

20. Bukovsky, J.: Psorospermosis follicularis vegetans, Arch. f. Dermat. u. Syph. **75**:279, 1905.

than primary changes. However, on careful analysis, it would seem that some of the vesicle formation in Bukovsky's case was similar to that in ours. Spiethoff [21] expressed the conception that vesiculation with lacunar formation indicated the essentially exudative character of the disease. Pohlmann's,[22] Reenstierna's [23] and Fernet and Scheikevitch's [24] reports were concerned with a complication also of acute eczema or impetigo. This admixture of engrafted disease apparently was present in the case reported by Spitzer,[25] as well as in that of Hudelo, Bigot and Caillau.[26] Louste and Barbier [27] recorded vesicopustules and small bullae in addition to classic lesions of the disease.

Buzzi and Miethke [28] regarded the lacunas as vesicles resulting from an exudative process, since they observed fibrin and lymphoid cells therein, as well as free hemoglobin in the corium. Because the rete cells always showed degenerative changes, these authors expressed the belief that the lacunas are not artefacts, contrary to the belief of Petersen.[29] However, they expressed the belief that such microscopic vesicles do not produce classic vesicles like those in pemphigus, on account of the pressure of the overlying horny plug.

Crosti [30] noted that acute eczema caused the lesions to assume, from time to time, an abnormal bullous character, which always led finally to dyskeratosis.

Hidaka [31] studied 8 cases exhaustively. He insisted that the primary lesion was a fleck or papule of the size of a millet, sharply

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21. Spiethoff, B.: Beitrag zur Pathologie des Morbus Darier, Arch. f. Dermat. u. Syph. **109**:197, 1911.

22. Pohlmann, A.: Dariersche Erkrankung in drei Generationen, Arch. f. Dermat. u. Syph. **97**:195, 1909.

23. Reenstierna, J.: Dariersche Dermatose mit Schleimhaut Veränderungen und impetigoartigen Eruptionen, Arch. f. Dermat. u. Syph. **124**: 841, 1918.

24. Fernet, P., and Scheikevitch: Un cas insolite de psorospermose, Bull. Soc. franç. de dermat. et syph. **26**:166, 1919.

25. Spitzer, R.: Zur Kenntnis der Darierschen Krankheit, Arch. f. Dermat. u. Syph. **135**:362, 1921.

26. Hudelo, Bigot and Caillau: Dyskératose folliculaire (maladie de Darier), Bull. Soc. franç. de dermat. et syph. **28**:159, 1921.

27. Louste, A., and Barbier, G.: Dyskératose folliculaire congénitale (maladie de Darier), Bull. Soc. franç. de dermat. et syph. **24**:130, 1922.

28. Buzzi, F., and Miethke, F.: Ueber die Dariersche Dermatose, an der Hand eines selbst beobachteten Falles, Monatsh. f. prakt. Dermat. **12**:9, 1891.

29. Petersen, W.: Ueber die sogenannten "Psorospermien" der Darier'schen Krankheit, Centralbl. f. Bakt. **14**:477, 1893.

30. Crosti, D. A.: Osservazioni su di un caso di psoro-spermosi follicolare vegetante (mallattie di Darier); nota clinico-istologica, Gior. ital. di mal. ven. **62**:26, 1924.

31. Hidaka, S.: Studien über die Dariersche Dermatose, Zentralbl. f. Haut- u. Geschlechtskr. **17**:873, 1925.

bordered, irregularly rounded or angulated and gray. He considered all other developments, such as confluence, maceration, erosion, papillary proliferations and vegetations, vesiculation and pustulation, as atypical or merely secondary manifestations. This opinion is at variance with that of others, and, as was intimated by Brünauer,[5] it is not sufficiently flexible to take into account the varying types of essential lesions in any one special case and certainly not those differences which may exist between 2 or more cases of the disease, particularly when the cases are followed for a long time.

The case of Höfer [32] and that of Milian and Périn [33] were characterized by pyogenic or pustular complications. In the latter case the first evidence of the eruption was preceded by an impetiginous and pustular process. Darier discussed this case and expressed the belief that the pustules and bullae were folliculitids or impetigo and that their inflammatory evolution called forth the dyskeratotic process. This opinion was in accord with Bettmann's [34] studies, which suggested that a specific or peculiar inborn property of the skin in Darier's disease responds to trauma by way of changes specifically characteristic of this disease.

REPORT OF CASE

E. E. L., a Chinese, when first examined in June 1929, was 40 years of age and married and considered himself in good general health. He had been in this country twenty years, during which time he was a waiter. His father for many years before his death had suffered from a cutaneous disease the cause of which was unknown. The patient was one of four brothers, all of whom were living and well. He did not recall that any one in his immediate family suffered from a cutaneous disease in any way similar to his. His past history was unimportant. He had had gonorrhea some years previously. His habits were temperate.

The present illness had been of at least twenty-one years' duration. It began in the groins and spread slowly to other locations. The affected areas had usually been vesicular or moist, and there were periods of remission. Physical examination at that time showed nothing unusual except that he was undernourished. The blood pressure was 90 systolic and 60 diastolic and the Wassermann reaction (with three antigens) was negative. The blood count was normal, with a differential white cell count of 58 per cent polymorphonuclear leukocytes, 34 per cent small lymphocytes, 5 per cent large lymphocytes, 3 per cent eosinophils and no basophils. A gastric analysis revealed much mucus, 45 per cent total acid and 24 per cent free acid. Roentgen examination showed "old fibrosis of both lungs; nothing active." The gastroenterologic diagnosis was "very definite intestinal stasis and secondary to this probably mild toxemia."

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32. Höfer, K.: Morbus Darier bei Vater und Sohn, Zentralbl. f. Haut- u. Geschlechtskr. **33**:14, 1930.

33. Milian, G., and Périn, L.: Dyskeratose folliculaire (maladie de Darier) avec bulles, Bull. Soc. franç. de dermat. et syph. **37**:1280, 1930.

34. Bettmann: Ueber Umbauvorgänge als Ausdruck spezifischer Reaktionsfähigkeit bei Hautkrankheiten (Die Reizbarkeit der Haut bei der Darierschen Krankheit), Arch. f. Dermat. u. Syph. **135**:65, 1921.

The eruption at the time of this examination was present on the neck, in the form of a patch, in the umbilical region, in the groins, on the scrotum and penis, in the perianal region and on the feet and toes, including the webs, and there were some suggestive ungual changes. On the shoulders, the flexures of the elbows, the chest and the back there were areas which were considered to be those of a fading dermatitis. The lesions in the groins and the perianal region were lichenified and somewhat fissured. There were occasional superficial ulcerations or denudations with crusting. There were no lesions in the mouth, and a Nikolsky sign was not demonstrable. Histologic examination of a specimen from the abdomen showed a thickened rete and a spreading of the cells near the basal layer, forming "lakelike areas." In some instances the entire upper layer of the rete had separated from the basal layer. It is interesting that no elements suggesting *corps ronds* or grains were recognized or noted.

Later observations were made at infrequent intervals, when the patient constantly presented vesicles or small bullae with a tendency to remission and relapse in certain areas. These were so prominent that a diagnosis of some type of toxic bullous erythema or of pemphigus vegetans was entertained. For this reason a general physical survey and a search for foci of infection were carried out in June 1935. A gastrointestinal examination, including roentgenograms, revealed a spastic pylorus and bowel; chronic tonsillitis was present, and a basal metabolic rate of —21 per cent suggested mild hypothyroidism. There was chronic constipation, the severity or relief of which had no effect on the cutaneous disease. Because he suspected from experimentation that the condition of his skin became worse at least from taking fried or boiled meats, candy, oranges, tomatoes and strawberries, he restricted his diet principally to fish, string beans, white bread and pork chops. The blood pressure was 100 systolic and 80 diastolic. Examination of the urine showed no abnormality. The Wassermann reaction was negative, and the blood count showed 89 per cent hemoglobin and 8,250 leukocytes with a normal (differential) smear. With hematocrit the sedimentation rate was 10 mm. in one hour and the volume of packed red blood cells 41 cc. and of packed white blood cells 0.2 cc. per hundred cubic centimeters of blood. A roentgenogram of the chest showed the lungs to be clear of active disease.

Shortly after these examinations the patient disappeared from observation and was not seen again until November 1936. He stated that in the interval he had received treatments "for his blood" without any change in the condition of his skin. These treatments consisted of intravenous injections of an arsenical preparation and intramuscular medication with a bismuth preparation at weekly intervals, with some irregularity, for one year.

At this time (November 1936) a restudy of the original biopsy material disclosed to us the true nature of the cutaneous disease, primarily on account of a clearer interpretation of the epidermal space formation.

Laboratory studies now revealed 6,750 white blood cells, with a differential count of 1 per cent juvenile neutrophils, 81 per cent segmented neutrophils, 9 per cent young lymphocytes and 8 per cent monocytes. The basal metabolic rate was —15 per cent. His blood fell in group III (Moss), or B (Landsteiner). Phytopharmacologic tests of the blood on two occasions showed readings of 50 per cent and 61 per cent, both toxic. This was of some interest. Patch tests with starch, soap, etc., gave negative results. Roentgenograms of the entire skeletal system showed no abnormality. We noted that cultures, on ordinary mediums, of vesicular contents of two of eight lesions were sterile in two instances and in six showed only white staphylococci.

Dermatologic Examination.—The patient was slender, somewhat stooped and fairly well developed but poorly nourished. He had typical Chinese facial traits, with a heavy crop of sleek black hair. Both legs revealed pronounced varicosities of the veins, extending to the thigh on the left. Aside from slight pityriasis the scalp was normal. The skin generally was of the normal oriental color and coarseness, rather smooth and slightly oily. The palms were slightly dry and scaly, and the soles showed increased redness anteriorly, with some dryness and faint scaling. All the nails were intact.

Fig. 1.—Vesiculation and crusting are conspicuous on the abdomen and on the groins; the flexures of the elbows are involved to a lesser degree, and many discrete and grouped lesions are present on the arms and the upper part of the trunk. Most of these reveal crusting.

The most striking and typical lesions were located on the abdomen, which was the area of most extensive involvement, in the axillas, groins, perianal region and flexures of the elbows and on the sides of the neck extending slighlty toward the shoulders. A large patch with an irregularly indented, gyrate and occasionally serpiginous outline extended across the abdomen, its largest transverse diameter reaching from one anterior axillary line to the other and its longitudinal diameter from the level of the xiphoid process to a line connecting points about 4 inches (10 cm.) above the groins. The patch was composed of coalescent slightly infil-

trated purplish red papules of delicate, soft texture, their bases usually being broader than their tops. They varied in size from that of a pinpoint to that of a match head, the average size being that of a pinhead, and they showed no uniformity of shape. They were mostly angulated, flat topped or truncated, but some were smoothly or irregularly rounded. Throughout this large patch there were a few small islands of normal skin. In a diffuse area of this type the nature of the papular process could be determined in certain spots only and during certain periods, because most of the time the entire surface was covered with dry or moist yellowish crusts or with a thin but resistant grayish corneous membrane. It was the presence of this semiopaque membrane and the conspicuous absence of real keratinization which constituted the peculiarity of the lesions. This membrane apparently was formed above the coalescent papules as a uniform, smooth gray sheet. In isolated areas it was thinned, less opaque and flaccid, forming blebs containing both clear and turbid fluid. These vesicles were discrete and grouped.

A vesicle could reach extensive diameter by continuous uplifting of the membrane in any particular portion of the patch but was most often limited in its evolution by early rupture from scratching because of pruritus or by accidental friction caused by clothing. Since a vesicle was formed by the separation of a preformed membrane, it was obvious that its borders would be, as a rule, indistinct and irregular. There appeared occasionally a well rounded-out and circumscribed pemphigoid vesicle. When the slightly wrinkled top of a developing bulla was removed, a clear fluid was released, and a smooth brownish red or red raw surface was exposed; this continued to seep even after repeated sponging. When the lesion was undisturbed, a grayish crust formed, and changed to yellow. If further erosion took place within the exposed smooth raw surface, an uneven groundwork of tiny brownish red somewhat granular and moist papillary projections was revealed underneath. This became dry, with the formation of a faintly perceptible crust.

Because of this constant vesicle or bleb formation with rupture, on most of the surface of the patch on the abdomen there were yellowish adherent crusts interspersed irregularly with smooth grayish membrane-covered infiltrated zones, some with fresh, wrinkled vesicular tops. Where healing began, one noted a stoppage of membrane formation, and the surface presented a faintly lichenoid reddish brown papular appearance, which gradually flattened and finally effaced itself, leaving a dry, diffuse or mottled brownish pigmented normal skin. Reactivation occurred later in these healed areas.

On each side of the neck extending slightly to the shoulder there was an irregular, ill defined palm-sized patch the appearance and evolution of which were similar to those of the lesions of the abdomen. Pinhead-sized barely elevated brownish red flecks and elevated papules, for the most part coalescent in patches, formed an overlying membrane. Repeated uplifting of this by vesicles which ruptured, oozed and crusted caused the patient extreme annoyance. In the axillas, groins and perianal areas the patches appeared on the apposing surfaces, and aside from the added factors of functional irritation, moisture, crusting and erosion, they were essentially the same as the lesions on the abdomen and the neck. Because of macerative factors, intact vesicles were rarely observed, but there was no tendency to verrucoid or vegetative changes. During the period of study a patch of the aforementioned type appeared occasionally in the flexure of each elbow.

Over the entire trunk, from the shoulders to the groins, and on the arms there were irregular mottled areas of dirty light or dark brown pigmentation. Scattered about, but with no special symmetry, were tiny lesions consisting of a few grouped

one observed always a distinct disruption or cleavage of the cells to form definite spaces or lakelike areas, which were well lifted up, or a partial tearing asunder of the lower rete cells, giving rise to linear, almost horizontal, clear areas, affecting as many as six or seven rete pegs.

The larger lacunas were apparently extensions of many small or large disruptions of the rete cells.

Wherever one or several layers of cells composed the floor of a lacunar space, they appeared disorganized and showed a tendency to separation from one another, together with loss of spinous processes.[35] Where detached, these cells appeared as rounded elements, with a sharp, deeply staining rim of protoplasm surrounding a clearcut nuclear membrane. The nuclear substance was reduced in some instances to a shrunken, darkly staining spot. Thus the picture of *corps ronds* and of grains, so well known, was not conspicuous but merely suggestive.

The other changes in and around the basal cell layer were consistent with those usually observed. There was an increase in the pigment cells. The finger-like arrangements of the pegs produced occasionally a clumped effect at their bases, where they proliferated into the corium. Openings or small clefts among the cells were well depicted, but spongiosis was not seen. Many of these cells apparently took on increased basophilic staining.

Some sections showed tinctorial changes in the basal cells, which might be viewed as significant (fig. 2). With Masson's trichrome stain the earliest changes in the epidermis appeared to be in the basal layer zone, where there was hyperactivity of cells, revealed by increase in size and by mitosis. Such cells took on a slightly deeper basophilic stain than did the squamous cells lying above them.

Contents of Spaces and of Vesicles: It was interesting to note that cleavage spaces were present, with a thin roof of squamous cells, and that in some sections definite vesicles appeared above such spaces (fig. 3). The contents of these spaces and vesicles[36] differed in some respects, viz.:

Lacunas were for the most part free of any inclusions or of cells other than those forming the basal layer and lying free within the spaces. Occasionally a hyaline-staining amorphous mass and a few red corpuscles were observed.

The vesicles contained in whole or in part similar amorphous masses of a coagulum suggesting fibrin, and the cells were chiefly polymorphonuclear leukocytes, with a few lymphocytes, an occasional eosinophilic leukocyte and granules

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35. Whether these fissures and lacunas resulted from mechanical disruption either in performance of the biopsy or in fixing of the specimen was discussed in great detail by Brünauer.[5] The proponents of the theory that they are artefacts were answered by Kreibich (cited by Brünauer,[5] p. 253), who asserted that fixation of normal and of pathologic skin other than that affected by keratosis follicularis, did not in his experience produce these lakelike and fissured areas. It should be noted in this connection that the "roof" and the bottom layer of these characteristic areas of separation apparently would, if approximated, fit into one another almost perfectly, thus leaving little doubt of there being a separation or disruption. Whether this fissuring is an artefact or whether there existed in vivo a potential weakening or loss of cohesion among the basal cells, we were inclined to view this phenomenon as the most important criterion in the diagnosis.

36. In one instance when a vesicle was superimposed on a definite lacuna a communication between the two was observed. This naturally raised the question of the vesicles perhaps arising from a fissure or from a lacuna. This point has not been settled in our opinion, but it seemed significant that the contents of vesicles and of lacunas were not uniformly the same.

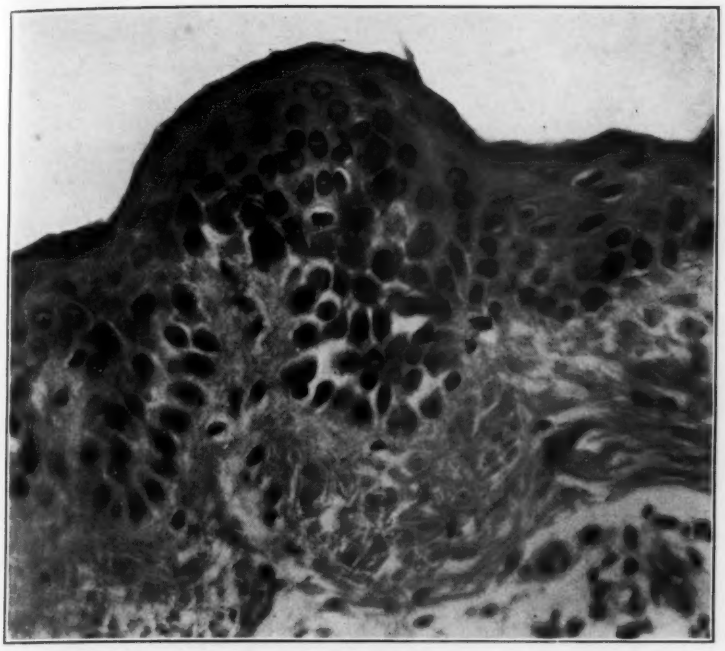

Fig. 2.—High power magnification of the fifth specimen. The rete is beginning to proliferate downward. The lowermost cells reveal loss of cohesion (space formation and fissuring) and take a deeper basophilic stain. In addition, there is beginning mitosis. *Corps ronds* and grains are not seen.

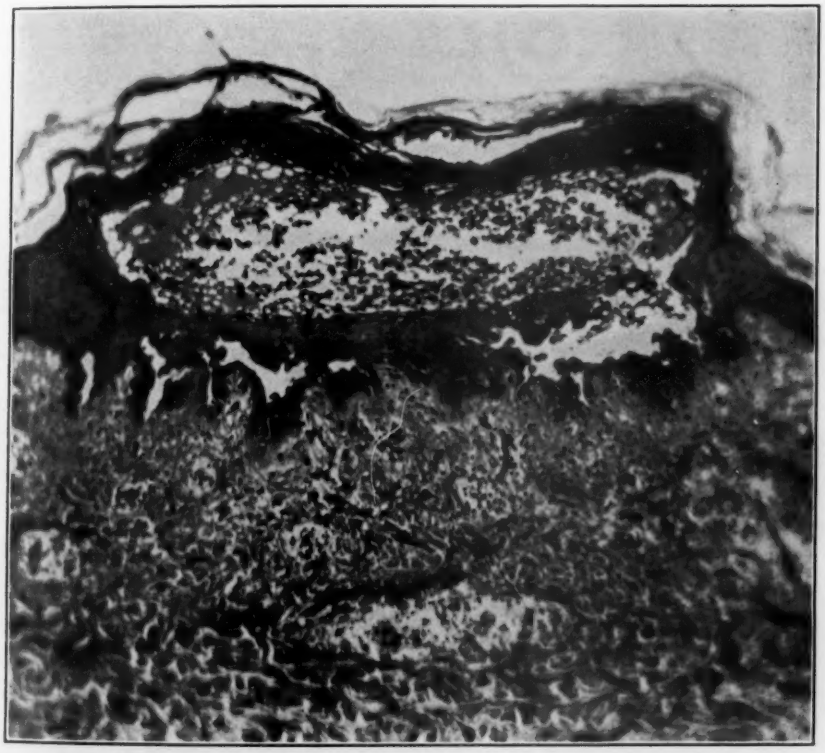

Fig. 3.—Low power magnification, showing a vesicle and, below it, lacunas. The floor of the vesicle is a portion of the rete layer; at one end there is a communication between the vesicle and the lacuna. The projections of the rete into the corium may be readily seen.

either in masses or in groups loosely arranged. As stated before, rounded basal cells and merely suggestive *corps ronds* and grains were present. In some instances, however, the same type of fibrin-like or amorphous material was found in both lacunas and vesicles. This was significant with respect to the relation of, or direct connection between, vesicles and lacunas and further suggested a possible rupture of the cells separating the two types of space formation.

In the corium there was dilatation of the lymphatic vessels—perhaps more than of the blood vessels—and moderate perivascular infiltration consisting principally of lymphoid cells, a few polymorphonuclear leukocytes, an occasional large mononuclear cell, fibroblasts and eosinophils. Moderate uniform edema was noted, especially about the perivascular infiltration. In some sections dilated capillaries filled with red corpuscles and separated by edema were evident, very close to the rete pegs. The adnexae were apparently normal; sweat glands were rarely seen and were normal, and the elastic and collagenous structures were not disturbed.

COMMENT ON PATHOGENESIS

From our own studies and the views expressed in Brünauer's monograph, we are inclined to the belief that the primary and essential changes in Darier's disease occur in the epidermis.

Any consideration of the origin of *corps ronds* and of grains is superfluous, since these bodies are present in other diseases and accompany the general upset of keratinization known as dyskeratosis. Keeping in mind the added characteristics of moisture up to vesiculation which may be predominant in some cases, one should note that the dry, crusted and hyperkeratotic types of the disease are customarily considered classic.

Since we have found from examination of various specimens taken from these classic types, as well as from our own patient, that changes in the rete and particularly in the basal cell layer are uniformly present, we shall discuss these in some detail.

Examination of many sections from any one block of tissue will show minute changes which become more definite and pronounced and eventually portray the uniform characteristics which we desire to emphasize.

At first one sees abnormalities of the rete cells, both tinctorial and morphologic. The cells apparently lose their normal cohesion, and slits or cleavage spaces form. At the same time (fig. 2) perceptible hyperplasia is taking place, resulting in a multiplication of the basal and prickle cells. As the apparent disturbance of normal keratinization progresses, the epithelial cells, retaining an intact palisade formation, begin to show small areas of cleavage, leading to disruption. The degree or extent of this is apparently governed by forces or conditions as yet not understood.

Continued abnormal keratinization now shows what every one recognizes as dyskeratosis. *Corps ronds* and grains may be seen or, as in our case, may be only suggestive or actually absent.

At this stage, where minute or definite space formation is evident, it is conceivable that the lymph or any other fluid present in the normal structures has been disturbed, with perhaps an increase in content. Whether such spacing or disruption is potentially present in vivo—a concept to which we are partial—is, of course, speculative. (One of us [M. H. G.] attempted to demonstrate this by means of frozen sections, with inconclusive results.) In this early stage one can discern nublike or finger-like processes projecting into the cutis and perhaps hyperkeratotic changes in the horny layer, with or without *corps ronds*

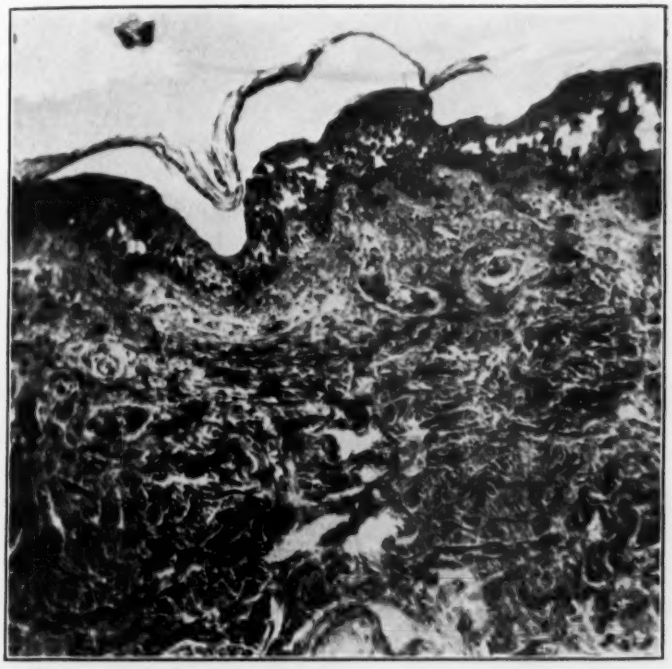

Fig. 4.—Low power magnification, showing slight hyperkeratosis, definite acanthotic changes with deeper staining and, particularly, fissure and lacuna formation in the lower layers of the rete.

and grains (figs. 3 and 4). These appear to arise in rete cells just above the intact basal layer.

From this stage of evolution the element of vesiculation becomes apparent. The fissure formation becomes more pronounced and leads to lakelike areas, or lacunas, the latter being merely an exaggeration of the process. In the usual type of Darier's disease the fluid which is present in vivo in lacunar areas presumably filters through the interspinous spaces and reaches the surface, forming crusts which have been described by all observers. This penetration of fluid is due, probably,

to the character of the surface of the rete: the presence of parakeratosis, *corps ronds* and grains in addition to increased keratin. Trauma, pruritus and infection appear in this stage to play some role in the production of vesiculation.[37] The appearance of a vesicle, either as a lacuna or, as we found it (fig. 3), located above a lacuna and possibly partially connected with it, is not readily explained, because the contents of vesicles and of lacunas differ somewhat. We are inclined to the suggestion, however, that there is some relation between them. Vesicles in our case appeared only on previously involved skin.

It should be noted that the changes recognized as dyskeratosis are seen among rete cells not in the lowermost, adherent layer, but in those directly above it. Furthermore, in our case the cells in lacunas and fissures gave evidence of premature keratinization, merely suggesting *corps ronds*, but in the main such cells were inconspicuous. They were not characteristic of *corps ronds* and grains, and they never formed typical keratoid masses, as in the classic examples of the disease. There were, nevertheless, many cylindric or columnar cells with a basophilic nucleus which resembled basal cells. Whether this lack of, or decrease in, formation of typical *corps ronds* and grains is associated with a tendency to early vesiculation is purely speculative.

On the basis of these facts and from study of additional typical cases of the disease we are inclined to think that the pathognomonic feature is not the occurrence of *corps ronds* and grains but, rather, of acanthosis, fissuring and lacunar spaces. It may thus be concluded that the essential and primary changes, as we have stated, occur in the lowermost portion of the rete. Our case, because of vesiculation, may serve as a basis for speculation on the forces which inaugurate this pathogenesis. A complete but inconclusive discussion of this was given by Brünauer. Whether the slowing down or speeding up of the process of transition of basal to prickle cell formation is the primary change, is, however, not clear. The hyperplasia of basal cells, acanthosis, disjunction of cells, formation of lacunas, vesiculation and dyskeratinization are, perhaps, the results of a peculiar force or agent.

We have thus partially indicated the march of events but can offer no further suggestion regarding causation. The peculiar makeup of the skin, a diathesis inherited or acquired, dysplasia of basal cells, the complication of secondary disease, trauma (Bettmann,[34] Darier [37]) and the presence of a toxin (phytopharmacologic test) all apparently deserve serious consideration.

SUMMARY AND CONCLUSIONS

1. A case of Darier's disease is reported in which vesicle formation was a prominent feature.

37. Darier, J., in discussion on Milian and Périn.[33]

2. Certain types of the disease may be vesicular in regions not subject to irritation, such as chafing and the like, or they may occur as the result of some possible complication or even accompany another disease of the skin.

3. Clinical diagnosis may at times offer considerable difficulty.

4. Histologic study is essential for the establishment of a correct diagnosis. What such a diagnosis demands is not always the presence of *corps ronds* and of grains but, rather the constant and consistent presence of acanthotic and disruptive changes in the rete at the lowermost layer of basal cells. These consist, we believe, first, in disruption of the individual cells through loss of cohesion, together with prolongations and hyperplasia downward; second, in changes in the basal cells themselves; and third, in the constant formation potential or actual, of fissures enlarging to lacunar development and later, in some cases, to vesiculation. This would explain the constant presence of crusting in some form in this unique disease.

5. It is suggested that the changes in the rete in the region of the basal cell layer are probably the initial steps in the pathogenesis of this disease and that the extent and degree of these changes determine the clinical picture.

Dr. L. W. Ketron assisted us by reading the manuscript.

ABSTRACT OF DISCUSSION

Dr. Lee McCarthy, Washington, D. C.: When Dr. Pels's case was presented before the Baltimore and Washington Dermatological Society last year, the original diagnosis of pemphigus was accepted by all. However, a routine biopsy showed the typical histologic picture of Darier's disease. When the patient was reexamined, other clinical signs of Darier's disease were noted. However, the interesting point about the clinical aspect of this case was the presence of numerous large bullae, especially on the trunk. The bullae appeared to arise from normal skin. The presenter has laid considerable stress on the presence of "corps ronds" and "grains" in diagnosing Darier's disease. These products of epithelial degeneration may be seen not only in the dyskeratotic group but in many other diseases, such as blastomycosis, pemphigus and bromoderma. It is difficult to explain the extensive bullous formation in this case. which is an unusual manifestation. From the histologic point of view it is surprising that vesicles and bullae are not seen more often, for separation and dissolution of the upper portions of the epithelium are the rule in cases of this disease. Perhaps Dr. Pels can venture some opinion about the origin of the bullae in this case.

Dr. Clark W. Finnerud, Chicago: I have never been convinced that such spaces are the result of edema in the epidermis. They are essentially the same spaces that one sees in lichen planus, the so-called Max Joseph Spaces.

Practically always one finds fissuring lacunas associated with the dyskeratoid changes. Furthermore, I cannot understand how the lacunar spaces are the

result of primary edema or edema in the epidermis. There should be no noteworthy change in the papillary portion of the corium and no sign in view of the chronicity of the condition.

Dr. Fred D. Weidman, Philadelphia: Whether this vesicular condition is the same as Darier's disease depends first and foremost on what the original description of Darier's disease was. As much as possible one ought to follow the custom of the biologists and accept as diagnostic features those which were originally described. That is, considerations ought to obtain in the nomenclature of disease as for the agents which cause disease. After that, if there are variants to be claimed the most reasonable and most valuable way of showing the relations is by demonstrating similar or identical etiologic factors; therefore, if additional features can be established it marks an advance in knowledge of the symptom complex. However, in the absence of a known cause for Darier's disease, the question as to whether the vesicular form belongs to it will depend on how many of the items in its symptom complex can be observed in this patient and found to conform with the original description (diagnosis) of Darier's disease.

In Dr. Pels's case there are so few clinical observations which suggest Darier's disease that the histologic changes alone should not be regarded as diagnostic. Both Dr. Pels and I have been studying sections from a patient in Birmingham, Ala., whose dermatosis clinically suggested chronic recurrent pemphigus or bullous erythema multiforme. Dr. Pels regarded it as atypical (bullous) Darier's disease, on the basis of the deep epidermal cyst formation seen microscopically. The cysts were identical with those observed in Darier's disease, but since there were not any associated keratinizing changes I would not agree.

Dr. Isaac R. Pels, Baltimore: Dr Goodman and I have been interested in this aspect of the pathologic picture of Darier's disease, because we studied about 8 other cases, and every one of them fulfilled the criteria which I have endeavored to outline.

It is interesting that in at least 3 instances, 1 of the patients being referred to Dr. Weidman, the same histologic picture was observed. There was clinical vesiculation of the lesions, but the condition, in our opinion, was not pemphigus.

It was stated that at first we believed the patient to have an unusual type of pemphigus, but we were not inclined to entertain that diagnosis after we had come to some conclusion from the histologic pictures.

In answer to Dr. McCarthy, who saw our patient, we studied 2 other patients, just referred to, with the same histopathologic picture; but they presented an entirely different clinical aspect. I believe, however, that if one makes careful examination in such cases (with vesicular lesions) one will find an almost nondescript type of eruption, namely, what our patient presented—a crusted membrane which tends to shrivel up. The first thing one thinks of in this case, then, is pemphigus. The histopathologic picture in cases of Darier's disease, however, is usually uniform.

As for the fissures being artefacts, that is discussed at length in Brunauer's monograph, and I merely cite Kreibich's comment that in his experience he has not found such fissures after making biopsies of material from normal or from any other type of skin.

I think Dr. Michelson's point was more or less stressed when I spoke of pemphigus vegetans. We found one histologic picture in Kyrle's book that did show space formation and lacunas which might have passed for this picture (Darier's disease). However, it did not reveal the other changes in the basal layer which characterize our case.

I believe Dr. Finnerud brought up the question of the vesicles being connected with the lacunas. This is still problematic. We found that the contents of the vesicles and those of the lacunas differed somewhat. Although I did not take time to mention it, we found that the vesicles contained lymphocytes, polymorphonuclear leukocytes, some eosinophils and some mitotic cells and granules. They were not quite similar in their contents to the lacunar spaces, although one noted that connections existed between spaces and vesicles.

Finally, Dr. Weidman brought up the question of the clinical aspects and what Darier had originally described. As a matter of fact, in Darier's second communication he particularly stressed the fact that the lacunar formation was a prominent change, but he did not pay as much attention to that as to the formation of the classic "corps ronds" and "grains."

I feel, therefore, that when attention has been called to this one feature—fissure formation—the diagnosis of Darier's disease can and must rest on thorough histologic examination.

TUBERCULOID LEPROSY

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The interesting paper read at the last meeting by Dr. Lehmann [1] on unusual manifestations of leprosy and Dr. McCoy's [2] dissertation on the communicability of this disease have led me to offer some remarks on tuberculoid leprosy.

The lesions in which histologic examination reveals a tuberculoid structure are frequently unrecognized or erroneously diagnosed because of their noncharacteristic clinical aspect and the discreteness, there being sometimes from one to three plaques, often of a monoform aspect. The use of the term "tuberculoid" to indicate this type of leprous lesion has been criticized by some authorities, and certainly the term is open to objection; but since it has been accepted by most writers on leprosy and since no better name has been proposed to replace it, I shall continue to use it.

Owing to the absence or scarcity of Mycobacterium leprae in tuberculoid lesions, there has been a tendency—at least until recent years—on the part of various authors, especially Neisser [3] and Lie,[4] not to accept such manifestations as conclusive evidence of leprosy but to consider them a possible complication of lupus. There has been no verification of this point of view: tuberculin reactions have been negative, and experimental inoculations of animals have given negative results. In this connection it is important to mention the following conclusion of Mitsuda and Ogaya: [5]

> Tuberculosis-like changes in the viscera have no relation to the tuberculoid changes found in the tuberculoid macules of the skin; such visceral changes are only a manifestation of generalized tuberculosis.

Read at the Sixty-First Annual Meeting of the American Dermatological Association, Inc., Del Monte, Calif., June 9, 1938.

1. Lehmann, C. F.: Leprosy: A Review of Some of Its Unusual Features, Arch. Dermat. & Syph. **37**:175 (Feb.) 1938.

2. McCoy, G. W.: Communicability of Leprosy and Application of Control Measures, Arch. Dermat. & Syph. **37**:169 (Feb.) 1938.

3. Neisser, cited by Darier, J.: Les tuberculoïdes de la lèpre, Conf. internat. de la lèpre, 1924, p. 180.

4. Lie, M., in discussion on Pautrier, L. H., and Boëz, L.: Cas de lèpre tuberculoïde, Conf. internat. de la lèpre, 1924, p. 188.

5. Mitsuda, K., and Ogaya, M.: A Study of One Hundred and Fifty Autopsies on Cases of Leprosy, Internat. J. Leprosy **5**:53 (Jan.-March) 1937.

Since 1934 the conception of Boeck's sarcoid has been changed and designated by the Strasbourg (France) school as Besnier-Boeck disease.[6] In view of the work and synthesis of Schaumann, it is accepted as a proper entity, an expression of reticuloendotheliosis of the organism in which the cutaneous manifestations are inconstant and in which the ganglionic manifestations predominate by their frequency and importance. These lesions present a histologic aspect considered by some authors as specific, accompanied at times with variable osseous changes, sometimes with Jüngling's osteitic cystoid type. All these facts give to the tuberculoid manifestations of leprosy a new and greater interest, if it is considered that the process in some cases affects the reticuloendothelial system of the skin, lymphatic glands, bone marrow and spleen and produces with significant frequency cutaneous lesions of a marked sarcoid appearance. It will suffice to mention the famous case presented at the International Congress of Dermatology and Syphilology in 1900, which eminent dermatologists like Balzar, Danlos, Hallopeau and Darier diagnosed as an instance successively of "dermatosis indeterminata," "tuberculid multiforme" and "granuloma of a new type." Finally Boeck himself, who examined the patient, pronounced the disease to be leprosy.

Reading of Boeck's original text, in which he analyzed 1 of his cases of sarcoid, reveals that as the examination took place "on a dull April morning" a diagnosis of leprosy was made. Some time later the patient was seen by Hansen, who examined a preparation made from an enlarged epitrochlear gland. He was doubtful about the diagnosis, as the clinical appearance did not conform to the histologic structure. This happened in 1905, seven years after Jadassohn [7] had pointed out the presence of a frankly tuberculoid structure in lesions of cutaneous leprosy.

Later it was shown that tuberculoid leprosy may be found in lymphatic glands, nerves and viscera, where it is so similar to sarcoid as to make it impossible to differentiate rhinitis leprosa from rhinitis accompanying Besnier-Boeck disease in cases in which Mycobacterium leprae cannot be demonstrated.

In leprosy one may observe generalized and discrete adenopathy, lesions at the hili of the lungs and osseous alterations that are not distinguishable from sarcoid, all these symptoms being accompanied with cutianergia tuberculinica.

Some authors, taking into account the importance of the foregoing facts according to which not only leprosy but tuberculosis and leishmaniasis may produce lesions of sarcoid structure, have rejected the

6. Gougerot, H.: Sarcoïdes: Syndrome et adjectif; multiplicité des causes; fréquence de la tuberculose, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **41**:1017 (June) 1934. Halkin, H., and Lapière, S.: Quelques cas de sarcoïdes, ibid. **41**:1021 (June) 1934.

7. Jadassohn, cited by Darier, J.: Les tuberculoïdes de la lèpre, Conf. internat. de la lèpre, 1924, p. 182.

etiologic identity of these lesions and have called them a syndrome[8] which occurs, in order of frequency, in tuberculosis, leprosy and mycosis.

HISTORICAL NOTES

The existence in leprous tissue of giant cells was pointed out years ago by Toma, Ramón y Cajal, Schaeffer and others; but in the structural details of nodular leprosy there is nothing to suggest the tuberculous process.

The original description of tuberculoid leprosy was given in 1898 by Jadassohn, who indicated the existence in certain cutaneous manifestations of a tuberculoid aspect, with follicles formed by Langhans' giant cells, epithelioid cells, lymphocytes and Mycobacterium leprae in reduced numbers. Later on Klingmüller,[9] Pautrier and Boëz[10] and Darier[11] reported similar observations. Arning,[12] Blascko, Klingmüller[13] and Schaeffer likewise noted the existence of a frankly tuberculoid texture in the nerves and various organs of patients affected with leprosy.

It was not, however, until the Third International Leprosy Conference, in July 1923, that Darier established conclusively the identity of the tuberculoid manifestations. From that time this knowledge has spread among dermatologists, who commenced to publish their observations, although not nearly so extensively as the subject merits. Besides the works already mentioned one should cite those of Seminario and Gavina Alvarado,[14] Rabello Jr.[15] and Motta[16] in Brazil; Schujman[17]

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8. Kissmeyer, A.: Contribution à l'étude anatomo-pathologique des sarcoïdes, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **41**:1278 (June) 1934. Pautrier, L. M.: Léprome à histologie de sarcoïde dermique, ibid. **41**:1284 (June) 1934. Dupont, A.: Leishmaniose cutanée à structure histologique de sarcoïde de Boeck, ibid. **41**:1291 (June) 1934.

9. Klingmüller, cited by Darier, J.: Les tuberculoïdes de la lèpre, Conf. internat. de la lèpre, 1924, p. 182.

10. Pautrier, L. H., and Boëz, L.: Lèpre tuberculoïde probable chez un Malgache (cas de diagnostic), Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **30**:57 (March) 1923.

11. Darier, J.: Les tuberculoïdes de la lèpre, Conf. internat. de la lèpre, 1924, p. 171.

12. Arning, E.: Veränderungen an den grösseren Nervenstämmen bei Lepra, Deutsches dermat. Kong., 1898, p. 57.

13. Klingmüller, V.: Ueber tuberkuloide Lepra, Arch. f. Dermat. u. Syph. **153**:584, 1927.

14. Seminario, C., and Gavina Alvarado, E. R.: Lepra tuberculoïde, Semana méd. **1**:1394 (May 30) 1929.

15. Rabello, Jr.: Données nouvelles pour l'interprétation de l'affection de Besnier-Boeck: Rôle de la lèpre, Ann. de dermat. et syph. **7**:571 (June) 1936.

16. Motta, J.: Les sarcoïdes de la lèpre, Ann. de dermat. et syph. **2**:1180 (Nov.) 1931.

17. Schujman, S.: "Lepra tuberculoide": Contribución a su estudio clínico e histopatológico, Prensa méd. argent. **22**:2504 (Dec. 25) 1935.

in Argentine; Tisseleul, in Madagascar; Soetopo, in Java; Reiss,[18] in China; Saburo, in Japan; Tebbuth, in Australia; Wade and Rodriguez,[19] in the Philippines and South Africa; Lowe,[20] in India, and Grau Triana and associates [21] and Sáenz,[22] in Cuba.

It must be understood that the term "tuberculoid" is used solely to describe the morbid anatomic picture; although a distinctive tuberculoid structure characterizes certain clinical manifestations of leprosy, the presence of tuberculoid leprosy can be determined only from the histologic changes and not, as erroneously claimed by some authors, from the clinical features, which may present a lupoid or sarcoid-like aspect.

To prevent false interpretation the terms lepra lupoidea and lepra sarcoidea must not be used for the histologic picture of tuberculoid leprosy. Nevertheless, the clinically lupoid and sarcoid-like forms of leprosy frequently present the tuberculoid structure to such an extent that, with certain experience, the condition may be suspected from the clinical picture and the suspicion corroborated by histologic examination.

Other manifestations of neural leprosy present nothing from the clinical standpoint to suggest a tuberculoid structure microscopically.

REPORT OF CASES

CASE 1.—A white woman aged 43 had first noticed an eruption seven years before I saw her. It consisted of a few scattered lesions on the chest, back and upper extremities. As the lesions were erythematous and without subjective symptoms, they were diagnosed and treated as chronic urticaria. The patient had always lived in a small country town where leprosy was endemic.

Physical Examination.—Only the lesions on the left arm and back were worthy of description, as the rest, about eight, disseminated over the chest, arms and forearms, were erythematous, ill defined, irregular in shape and not infiltrated. Only their persistence and coexistence with the elements on the back and arms aroused suspicion of their real causation. The lesion on the external aspect of the center of the left arm was irregularly oval and the size of a dime. That occupying the central part of the back was of the size of the palm. Both were irregularly outlined and faded into the surrounding normal skin. The center of the patches had a fine granular aspect, as if produced by tiny vesicles which did not contain liquid and were superficially infiltrated. Both had a reddish brown tint, showing anesthesia to light touch.

The Wassermann and the Meinicke reaction were negative. The von Pirquet test gave a negative result. Roentgenograms of the lungs, hands and feet showed

18. Reiss: Tuberculoid Leprosy Amongst the Chinese, in Deliberationes Congressus dermatologorum internationalis, Leipzig, Johann Ambrosius Barth, 1936, vol. 2, p. 583.

19. Wade, H. W., and Rodriguez, J. W.: The Skin Lesions of Neural Leprosy: Observations in Cebu, Internat. J. Leprosy **5**:1 (Jan.-March) 1937.

20. Lowe, J.: A Study of Macules in Nerve Leprosy, with Particular Reference to the "Tuberculoid" Macule, Leprosy Rev. **8**:69 (April) 1937.

21. Grau Triana, J.; León, F., and González Peris, G.: Sobre un caso de lepra tuberculoide, Rev. de med. y cir. de la Habana **41**:359 (June 30) 1936.

22. Sáenz, B.: Sobre algunas formas de lepra poco frecuentemente observadas, Vida nueva **25**:322 (April 15) 1930.

no abnormality. Inoculation of guinea pigs gave negative results. Nasal smears and scrapings from tissue showed no bacilli.

Histologic Picture.—The epidermis was atrophic, with slight hyperkeratosis. The dermis showed total absence of papillae, condensation of connective tissue limiting the basal layer and an extensive and diffuse infiltration, consisting of round cells, epithelioid cells, connective tissue cells and plasma cells. The blood vessels and hair follicles were surrounded by round cells and epithelioid cells. Stains for acid-fast bacilli showed two isolated organisms.

Fig. 1 (case 1).—*A*, *B* and *C*, erythematous lesions of tuberculoid leprosy; *D*, pretuberculoid leprosy, showing extensive and diffuse round cells and epithelioid cells.

CASE 2.—A white woman aged 45 consulted me because of a lesion of fifteen months' duration. She had been treated with neoarsphenamine and a bismuth preparation for six months, during which time the lesion increased in size. The family as well as the personal history revealed no important data.

Physical Examination.—A single plaque located immediately above the left elbow was irregularly round and the size of a dime, composed of an upper small group of elements and a lower larger group, separated by a narrow bridge of normal skin. Two isolated lesions were observed on the skin bordering the smaller lesion. All were composed of tiny nodules of two sizes, the larger that of a pinhead, and the smaller one half of this size, closely aggregated and yellowish red. Distinct infiltration occupied the entire dermis, more pronounced and elevated

at the border of the patch. It had a pebble-like appearance, and at a quick glance could be taken for either Boeck's sarcoid or lupus vulgaris. No lupoma was detectable under the stretched epidermis. Hypoesthesia was pronounced.

The Wassermann and the Meinicke reaction were negative. The von Pirquet test gave a negative result. Roentgenograms of the hands and feet and of the lungs showed osseous changes of the early period of Jüngling's cystoid type and lesions of the glands at the hili, respectively. Inoculations of guinea pigs with fragments of tissue gave negative results. Nasal smears and scrapings from the nodules showed no bacilli in more than one hundred slides. The Mitsuda test gave a positive result.

Histologic Picture.—The epidermis was normal. The dermis showed an infiltration which consisted of rounded and scattered inflammatory areas in

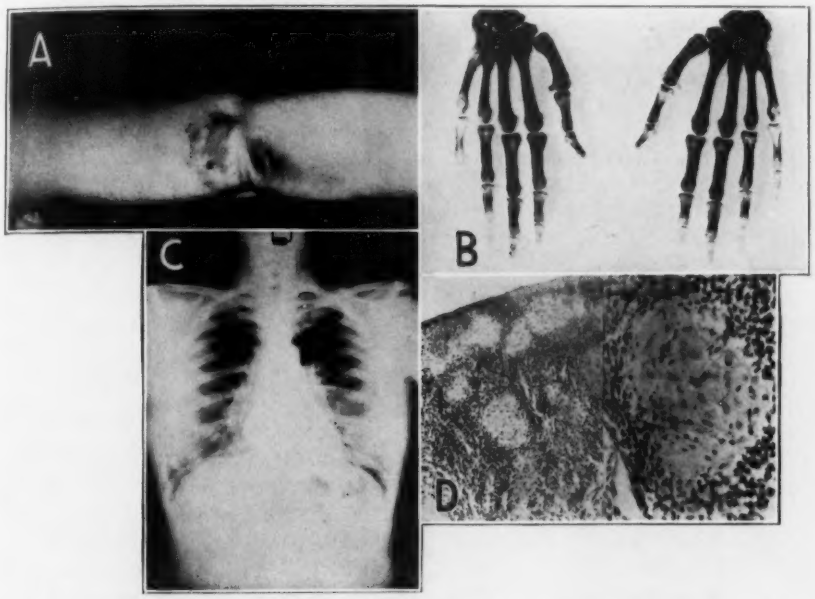

Fig. 2 (case 2).—*A*, solitary lupoid infiltration; *B*, roentgenogram of hands on March 14, 1936, showing osseous alterations; *C*, roentgenogram of chest, showing lesions at hili; *D*, low and high power magnifications of sarcoid-like infiltration.

the vicinity of the blood vessels of the papillary layer and corium, less pronounced in the lower part of the corium near the hypoderm. Some of the blood vessels showed dilatation and were partially obliterated by round cells. The periphery of the infiltrated masses consisted of lymphocytes and the center of numerous cells, represented in some places by pure epithelioid cells and in others by an admixture of epithelioid cells and elements that might represent an intermediate stage between histiocytes and epithelioid cells, the latter corresponding to an earlier period of the process. Epithelioid cells were predominant. The subepidermal disposition of the infiltration was characteristic, as narrow streaks or irregular masses not presenting follicular structure. This infiltration was present in the vicinity of organized structures: hair follicles, sweat and sebaceous glands, muscles and nerves. The demarcation of the connective tissue bordering the infiltration was sharp and appeared normal. The cellular infiltration and its architecture were

similar to that observed in sarcoid. No giant cells were present. As previously mentioned, the lesions in this case affected not only the skin but the reticuloendothelial system, causing alterations of the glands at the hili of the lungs as well as of the bones of the hands and feet.

Case 3.—A white woman aged 34 first noticed red patches on the left foot three years before examination, and a new lesion appeared six months later on the left upper extremity. Two members of her family had been affected with leprosy.

Physical Examination.—The lesion on the arm started above the elbow and extended down to the fingers, covering almost the entire extensor aspect of the limb. It was composed of two different types of elements. The upper third of the lesion consisted of a dull erythematous and partly pigmented patch; below this there was an area presenting a fine granular aspect, which sharply changed to the minute closely aggregated nodules observed in most of these cases. These pebble-like elements represent the most characteristic and frequently observed morphologic lesion of tuberculoid leprosy. Two special features must be pointed out: The sharply marginated border running along the radius suggested a neural distribution, and the small nodules had a flattened surface with superficial infiltration and a red-violet hue, more suggestive of lichen planus than of lupus vulgaris (this similarity being observed in the majority of cases). The ulnar nerve was enlarged and painful to pressure. Anesthesia, present in both lesions, was more pronounced in the upper one. The lesion on the medial anterior aspect of the right leg was oval, 7 cm. long and 2 cm. wide. The center was depigmented and atrophic. The surrounding skin was hyperpigmented. The border showed a granular aspect of brownish red and was slightly infiltrated. No lupoma was demonstrable. Hypoesthesia was present.

The Wassermann and the Meinicke test were negative. The von Pirquet test gave a negative result. Roentgenograms of the lungs, hands and feet showed no abnormality. Inoculation of guinea pigs with fragments of tissue gave negative results. Multiple nasal smears and scrapings of tissue showed no bacilli.

Histologic Picture.—The epidermis was distended and atrophic. The stratum corneum showed scaling without parakeratosis. The corium presented intense cellular infiltration occupying the entire thickness and starting immediately under the basal layer. The band of normal connective tissue located under the basal layer that is characteristic of ordinary lepromatous infiltration was lacking. In certain parts of the corium the infiltration took the shape of dense round masses, some exhibiting in the center typical giant Langhans cells. In some of these masses the infiltration showed a distinctive follicular structure; one or more giant cells were surrounded by numerous epithelioid cells and a ring of lymphocytes. This disposition was found in the upper as well as in the lower part of the corium.

The demarcation between the infiltration and the collagenous bundles of the dermis was sharp, as is the rule in leprosy. The elastic tissue was conserved. One interesting feature was the absence of necrosis in this type of infiltration. This may have been related to the scarcity of bacilli. Perivascular infiltration was observed, extending to the pilosebaceous glands.

Case 4.—A white woman aged 34 stated that three years previously she had first noticed a rounded reddish patch, which had slowly enlarged. Until five years before, she had lived with a brother who had nodular leprosy, and she came from a town where the disease was prevalent.

Physical Examination.—A solitary lesion of elongated oval shape, measuring 8 by 3 cm., was located on the lower external aspect of the left arm. The border was sharply defined and consisted of minute coalescent nodules, slightly raised and

infiltrated, of a reddish brown hue. In some small areas the nodular border was broken as the result of the absorption of the elements. The center of the patch was distinctly atrophic. The lesion closely simulated lupus vulgaris planus. Under diascopic pressure the nodules did not show the semitransparent aspect of apple jelly seen in lupoma, but faded completely, like erythema. Anesthesia to temperature and to pain was evident. The ulnar nerve was normal. Nasal smears showed no bacilli. In more than fifty scrapings from the nodules only a couple of acid-fast bacilli were observed.

The Wassermann and the Meinicke test were negative. The von Pirquet test gave a negative result. Roentgenograms of the hands and feet showed no changes on the bones, nor did those of the lungs show any changes in the glands of the hilus. Inoculation of guinea pigs with tissue gave negative results.

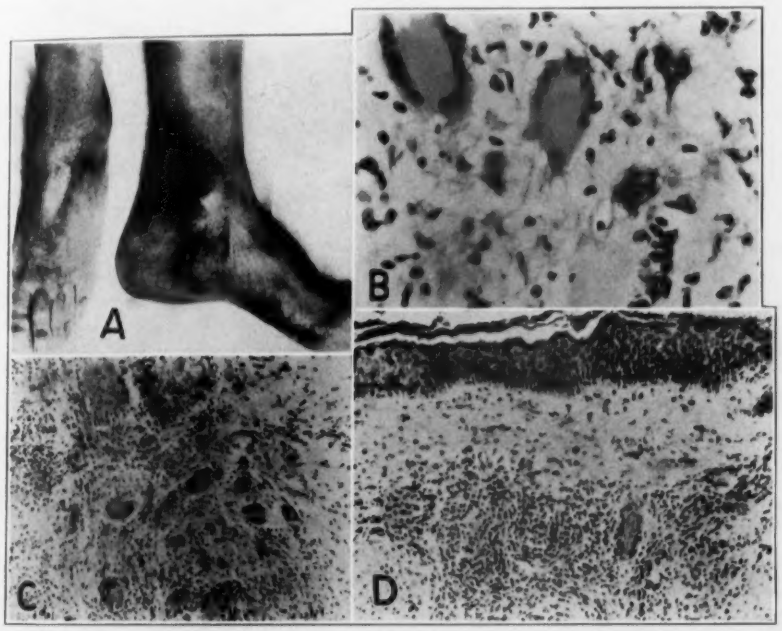

Fig. 3 (case 3).—*A*, achromic and hyperpigmented lesions; *B*, high power magnification of follicular infiltration; *C* and *D*, low power magnifications of follicular infiltration.

Histologic Picture.—Three biopsy specimens were removed from the active nodular elements bordering the lesion.

Fragments 1 and 2 presented the same histologic aspect. There was general atrophy of the epidermis. The central part of the slide was occupied by a voluminous rounded infiltration extending from immediately below the basal layer to the lower part of the corium. This nodule consisted of no less than twenty follicles, limited by collagenous tissue infiltrated by lymphocytes. Some of these follicles consisted of central epithelioid cells with surrounding lymphocytes; others presented a typical follicular structure, with Langhans giant cells at the center. The lower part of the infiltration showed the transverse section of a nerve, with perineural lymphocytic infiltration; thickening of the arterioles, all three coats being affected, and dense perivascular lymphocytic infiltration. The rest of the

dermis showed discrete nonspecific perivascular cellular infiltration. The diagnosis was follicular tuberculoid leprosy.

In fragment 3 the epidermis was slightly atrophic. The dermis exhibited a large infiltrated area, consisting of four adjoining nodules of pure epithelioid cells in the center, with surrounding lymphocytes. No giant cells were observed. Scattered epithelioid cells and lymphocytic infiltration were observed in the rest of the dermis. The infiltration was always limited by normal collagenous tissue; one of the deep nodules showed a thin nerve, with perineural infiltration, also extending to the nerve fibers. The blood vessels presented alterations similar to those observed in fragments 1 and 2. The diagnosis was sarcoid-like infiltration.

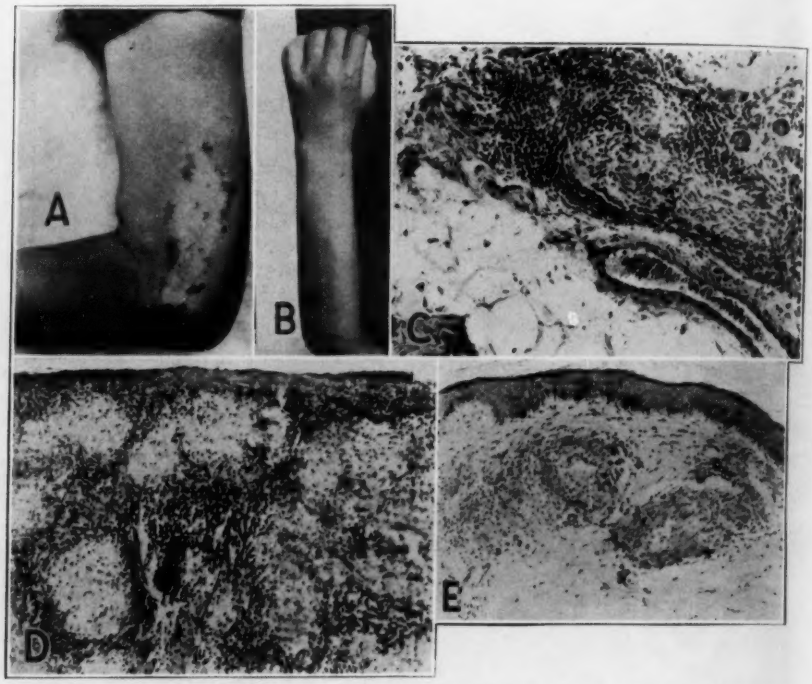

Fig. 4 (case 4).—*A*, solitary lesion with nodular border and atrophic center; *B*, lupoid infiltrated lesions; *C*, section showing perineural infiltration with vascular alterations; *D* (fragment 1), sarcoid-like infiltration; *E* (fragment 3), follicular infiltration.

CASE 5.—A white woman aged 37 first noticed an eruption two years prior to examination. She had received local treatment, without results. The family and personal history were irrelevant.

Physical Examination.—The lesion was located on the radial aspect of the left arm, immediately below the elbow, and consisted of a solitary round plaque, 1½ inches (3.8 cm.) in diameter, slightly raised and brownish red. In some areas small individual and aggregated nodules were observed; in other areas there was only pronounced infiltration. Anesthesia to light touch was more distinct in the center than at the border.

The Wassermann and the Meinicke test were negative. The von Pirquet test gave a negative result. Roentgenograms of the lungs, hands and feet showed no

abnormalities. Inoculation of guinea pigs gave negative results. Nasal smears and scrapings of tissue showed no bacilli.

Histologic Picture.—There were atrophy of the epidermis and appendages of the cutis, as well as pronounced infiltration of epithelioid cells immediately under the germinative layer and scanty giant cells with a follicular arrangement. The elastic fibers were rarefied. Special stains for acid-fast gacilli by the method of Ziehl and Klingmüller required many slides to demonstrate the presence of two organisms.

CASE 6.—A white boy aged 12 had been treated in the country for over a year, but, as the condition had remained unchanged, he consulted me. An uncle had been suffering from cutaneous leprosy. The past history was unimportant.

Physical Examination.—A solitary, erythematous and well circumscribed patch occupied almost the entire right cheek. The lesion was slightly infiltrated, more pronounced in the center and slightly raised above the surrounding skin. The color was dull copper red. Thin tiny scales were observed. The patient stated that the patch was numb, and pronounced anesthesia was observed. Two nerve branches of the right superficial cervical plexus showed distinctive inflammation.

Fig. 5.—*A* (case 5), solitary nodular patch; *B* (case 6), unique erythematous scaly patch; *C* (case 7), ill-defined achromic hyperpigmented lesions.

The Wassermann and the Meinicke reaction were negative. The von Pirquet test gave a negative result. Roentgenograms of the lungs and extremities showed no abnormalities. Inoculation of guinea pigs gave negative results. Nasal smears and scrapings showed no bacilli. The Mitsuda test gave a positive reaction.

Histologic Picture.—The epidermis was atrophied. In the dermis the papillae had disappeared. There was condensation of subepidermal connective tissue, presenting the shape of a narrow streak, which limited the upper part of the infiltration. The infiltration was profuse and abundant, assuming in some areas a round shape with a giant cell at the center, surrounded by epithelioid cells and bordered by lymphocytes—a follicular structure. In other places the cells were irregularly distributed, not following any special arrangement. The collagenous tissue limiting the areas of infiltration was normal. Special staining for acid-fast bacilli gave negative results.

CASE 7.—A white man aged 30 had noticed an abnormal condition two years before examination, but no changes in the skin had been observed before the lesions attained their current size. The family and past history were irrelevant.

Physical Examination.—On the posterior aspect of the left arm was a circumscribed achromic patch, partly annular and in part irregularly shaped. It was the size of a dollar and surrounded by café au lait hyperpigmentation, more pronounced in some areas than in others. There was no infiltration, scaling or elevation of the lesion. There were no subjective symptoms. On the right shoulder and on the back a few small scattered hyperpigmented and achromic spots were present. Anesthesia was distinct on the entire extensor surface of the arm. The other elements showed hypoesthesia.

The Wassermann and the Meinicke reaction were negative. The von Pirquet test gave a negative result. Roentgenograms of the hands and lungs could not be obtained. Inoculation of guinea pigs with fragments of tissue gave negative results. Nasal smears and scrapings of tissue showed no bacilli in over fifty slides. The Mitsuda test gave a positive reaction.

Histologic Picture.—The epidermis was normal. In places in the dermis there were absence of the papillae, condensation of the subepidermal connective tissue and cellular infiltration of the corium, which in some areas assumed a follicular structure consisting of central giant cells surrounded by epithelioid cells and bordering lymphocytes. In certain places giant cells, epithelioid cells and lymphocytes were distributed along the blood vessels and in the vicinity of the glands, muscles and nerves. Vacuolar alteration was observed in some of the epithelioid cells. Stains for acid-fast bacilli gave positive results.

Summarizing the histologic picture in the aforementioned cases: Three principal types of alterations can be differentiated in tuberculoid leprosy:

1. Pretuberculoid or subtuberculoid, as in case 1, corresponding clinically to fixed erythematous lesions.

2. Sarcoid-like, as in case 2, corresponding clinically to lupoid infiltrations. No acid-fast bacilli are observed, and there are coexisting alterations of the reticuloendothelial system.

3. Follicular, as in cases 3 to 7, corresponding clinically to lupoid infiltrations, erythematoscaling and achromic hyperpigmented lesions. Special staining methods showed reduced numbers of Mycobacterium leprae in these cases. In case 4 (biopsy specimen 3) the infiltration was of sarcoid type. No alterations of the bones or the reticuloendothelial system were observed.

A fourth type, called the neural abscess, frequently reported in India and Brazil, has not been observed by me in Cuba in over 500 cases of leprosy. Owing to the similarity of this type to colliquative tuberculosis, the name "colliquative" has been proposed.

Patients' statements regarding time of onset of the lesions and other features of the history have been carefully obtained, though I cannot vouch for their accuracy.

The biopsy specimens, of which in 1 case three were taken, have always been obtained by incision. For the histologic examination all specimens were divided into two fragments and both embedded in paraffin. One was fixed in Zenker's fluid and the other was fixed in solution of formaldehyde. In all cases, from six to twelve slides, all

serially cut, were stained by various methods. For demonstration of Hansen's bacillus, the blocks were sectioned completely.

SYMPTOMS AND DIAGNOSIS

From a clinical standpoint, leprosy of tuberculoid structure does not exhibit any characteristic dermatologic lesion that may lead to a definite diagnosis. In some instances there are:

1. An erythematous, infiltrated and sometimes scaling patch as an initial lesion. This gradually increases in size and becomes irregular in shape; later the center becomes paler and at the same time becomes fixed and undergoes retrogression.

2. A discoid solitary lesion composed of small nodules, resembling Boeck's sarcoid and lupus vulgaris but not showing any lupoma on diascopic pressure and resembling to a lesser extent small nodular syphiloderm or lichen planus.

3. Solitary, discrete and less often multiple annular lesions, with raised rough papular borders and depigmented atrophic centers.

4. Semicircular serpiginous lesions of the same type as the annular lesions.

5. Irregularly shaped and sometimes ill defined achromic nonscaly patches on a level with the surrounding skin, which may show slight hyperpigmentation in some areas. This type is usually located on the upper part of the back and arms.

That tuberculoid changes may be observed in the different clinical varieties of active leprid is strongly supported by the aforementioned findings, although there may be great variations in degree and different histologic pictures may be seen in the same patient at a certain moment or in the natural evolution of the condition. The common belief that the simpler forms of leprid are not tuberculoid may be due to failure of observers in the past to recognize the true nature of the minor degrees of the tuberculoid picture. Were all cases of leprosy studied histologically as a routine and not merely clinically and bacteriologically, as is generally done, doubtless the incidence of tuberculoid leprosy would be found to be much higher, and the transitional types between the pure macular forms, transient erythema, the achromic lesions and the lupoid infiltrations would be recognized.

There is one paramount and constant characteristic of all varieties of lesions: pronounced anesthesia to light touch with a needle on the center of the patch, sensation being sometimes preserved in the infiltrated border. The lesions never have any tendency to ulceration. Another important feature observed in the majority of these manifestations is the slow benign course of the lepromatous process.

Expression of a true infectious granuloma, the tuberculoid structure is the result of the action of the Hansen bacillus under varying biologic conditions, not differing in this regard from tuberculosis or syphilis. The early and retrogressing varieties are related to the pure macular forms, while pronounced infection is similar to the diffuse erythematous infiltration of lepromatous manifestations.

It is an accepted fact that tuberculoid leprosy is closely dependent on specific allergic processes, resulting in permanent clinical and histologic changes, the expression of an attenuated leprous infection that is produced by the defensive power of the host. Logically applicable to these leprous manifestations is the conclusion of Lewandowsky from experimental investigations on tuberculous infection: "The tuberculoid reaction is produced when the pathogenic agent is gradually autolyzed under the action of antibodies which represent the immunizing power of the organism."

The scarcity or absence of bacilli in the nasal secretion as well as in the cutaneous lesions, the benign course of the clinical manifestations not accompanied with febrile outbreaks, the occasional spontaneous regression of the lesions and the rapid and effective action of the treatment are features permitting one to consider tuberculoid leprosy as a mild type of classic leprous infection.

Furthermore, in my experience in over 35 cases of tuberculoid leprosy, I have never observed "lepra reaction." According to Wade and Rodriguez, this reaction occurs in 15 per cent of cases, and it may appear spontaneously or as the result of the administration of potassium iodide. The lepra reaction is frequently observed in severe forms of ordinary leprosy. The small incidence of this reaction and its quick regression when observed are arguments in favor of the defensive allergic power of the organism in the majority of cases of tuberculoid leprosy.

I emphasize once again that the diagnosis of tuberculoid leprosy must not be established on purely clinical grounds, owing to the absence of any constant dermatologic lesion.

The lupoid and sarcoid-like forms when observed in countries where leprosy is endemic may strongly suggest tuberculoid leprosy. The diseases that should be eliminated are: lupus vulgaris (no lupoma is detectable by diascopic pressure in tuberculoid leprosy); certain small nodular types of syphiloderm, the different forms of Boeck's sarcoid, and in rare instances lichen planus.

The possible confusion with Boeck's sarcoid is in some instances difficult to avoid. The clinical aspect and evolution of the lesions and the histologic structure may, as a rule, permit a definite diagnosis. In some cases investigation of these factors must be supplemented by thorough study of the lymphatic glands, lungs, liver and spleen and by roentgenograms of the bones of the hands and feet.

I have mentioned how difficult it can be to differentiate certain forms of syphilis from tuberculoid leprosy. The lupoid variety especially may be simulated by syphilis, and at times for a conclusive histologic picture a careful study of numerous slides will be required. In such instances only the treatment will solve the problem. Positive serologic changes cannot exclude leprosy in a patient with syphilis, but leprous manifestations are certainly not influenced by antisyphilitic therapy.

Cases in which the diagnosis is extremely difficult will require the aid of various laboratory procedures. Experimental inoculation of guinea pigs with fragments of tissue constantly give negative results, permitting one to exclude tuberculosis. Reactions to tuberculin tests are constantly negative, even with strong dilutions.

The Mitsuda immunobiologic intradermal test and other similar tests depend on an allergic condition. Some authors [23] have claimed positive results in 100 per cent of cases of tuberculoid leprosy, while other investigators [24] have denied the specificity of this test, which may give a negative result in cases of undoubted leprosy. They have expressed the belief that a positive reaction is indicative of the defensive power of the organism and of merely prognostic value. I have used the test in 5 cases, in only three of which it gave a positive result.

The results of investigation of Mycobacterium leprae in lymph from the lesions or at best in scrapings and by special staining of slides by the method of Ziehl and Klingmüller and of Gallego are not conclusive. The bacilli as a rule are scarce, and in some cases they cannot be demonstrated.

The histologic structure is of one of the four previously mentioned types. Its correct interpretation, in addition to the clinical findings, the absence of lupoma, the negative result of inoculation of guinea pigs, the endemic character of the disease and the anesthesia, furnishes sufficient evidence to exclude tuberculosis.

SUMMARY

A report is made of 7 cases of tuberculoid leprosy, 5 of women from 37 to 43 years of age, 1 of a man aged 30 and 1 of a boy aged 12 years. Four of the patients were from private practice and three from a dermatologic clinic, but all were well to do people of the middle class. All 7 were in good general health and had never had any febrile outbreaks (absence of lepra reaction). In all cases the course of the disease was slow, in some instances covering more than six years, the

23. Fernández, J. M.: El leprolin test, Rev. argent. de dermato-sif., May 1935, p. 108.

24. Boncinelli, U.: Ricerche ed osservazioni sulla reattivita cutanea dei lebbrosi alle cosidette "lepromine," Gior. ital. di dermat. e sif. **78**:629 (Aug.) 1937.

lesions not showing any rapid progression. In 2 cases the manifestations underwent spontaneous retrogression, and in some of the cases under my direct observation the lesions disappeared after appropriate treatment, proving their benign character. It must be emphasized that dermatologically there is no constant typical lesion of tuberculoid leprosy, the diagnosis being subject to determination by histologic means and requiring in some instances the use of various laboratory methods. Taken together, the findings in the aforementioned cases strongly support the view that tuberculoid changes are observed in all varieties of typical active leprid except true leproma, with variations in degree and in histologic details.

In my experience erythematoscaling, pigmentary achromic and macular lesions (minor clinical tuberculoid) usually correspond to undifferentiated infiltrations that are subtuberculoid or pretuberculoid histologically, while the papular and marginated elements (major clinical tuberculoid) are histologically represented in most instances by the tuberculoid or follicular type of infiltration.

Case offers proof that different histologic pictures may be found at a certain moment in the same case: specimens 1 and 2 were follicular and specimen 3 sarcoid. No repercussion on the reticuloendothelial system was observed.

If all cases of leprosy were studied histologically, as a routine, and not merely clinically and bacteriologically, as is usually done, the incidence of tuberculoid leprosy would doubtless be found to be much higher, and the ertnsitional forms between the purely macular lesions, transient erythema and the achromic hyperpigmented and lupoid lesions would be recognized.

Anesthesia or definite hypoesthesia of the lesions is constantly present as a major symptom.

The Mitsuda reaction is the expression of an allergic state and of little value from a diagnostic standpoint.

Mycobacterium leprae may be absent or present in small numbers in cases of tuberculoid leprosy.

ABSTRACT OF DISCUSSION

Dr. Howard Fox, New York: Dr. Sáenz apparently thinks that the presence of tuberculoid leprosy cannot even be suspected by the clinical appearance. In this regard I should like to cite the experience of Dr. H. W. Wade, of the Philippines, a man of enormous experience with this disease. Dr. Wade, in fact, made a tour of the world for the sole purpose of studying this phase of leprosy. I showed him three photographs of patients with such lesions, which I took while making a survey of leprosy in the Virgin Islands. He considered the lesions to be clinically typical of tuberculoid leprosy.

Dr. Braulio Sáenz, Habana, Cuba: The term tuberculoid is used solely to describe the morbid anatomic picture; although a distinctive tuberculoid structure characterizes certain clinical manifestations of leprosy, it can be determined only by histologic means. In some cases the clinical diagnosis may be suspected by physicians with a wide experience.

LXXXV.—TREATMENT OF LUPUS VULGARIS BY INJECTIONS OF STARCH U. S. P. (CORN STARCH)

REPORT OF A CASE

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ST. LOUIS

Chambers and Grand [1] have demonstrated that starch is a good chemotactic agent for leukocytes in tissue culture and in animals. It was suggested to me by Dr. E. V. Cowdry that the injection of this substance into the nodules of lupus vulgaris might be of therapeutic value.

PREPARATION OF MATERIAL

Starch U. S. P. (corn starch) was sterilized by baking at 150 C. in an oven, as suggested by Chambers and Grand.[1b] A 15 per cent suspension was prepared in a sterile rubber-stoppered vial, and only 10 cc. was made up at a time. This makes a heavy suspension which settles on standing. Fresh suspensions were made frequently to avoid contamination. A tuberculin syringe and a 20 or 21 gage needle were used. A smaller needle did not allow free passage of the material. The preparation was injected directly into the nodules at the edge of the lesion.

Six patients selected at random in the clinic were given intradermal injections of 0.1 cc. into the forearm and the reaction observed. Erythema and a papule were noted in each case within twenty-four hours, and in 1 a pustule appeared. This reaction slowly subsided.

REPORT OF CASE

J. C., a Negro aged 57, first noticed a lesion on his left cheek twenty-four years before he was admitted to the clinic (in February 1929). It had progressed slowly in size up to that time. It was the size of a man's palm, involving the left cheek and the lobe of the ear and extending down to the neck, just in front of the ear (see illustration). The lesion was nodular and was raised at the edges to a thickness of 2 to 6 mm. It was soft and irregularly shaped and presented several scaly areas. No evidence of tuberculosis elsewhere in the body was ever found. Histologic examination of the lesion showed a few giant cells, many epithelioid cells, lymphocytic infiltrate and necrosis typical of lupus vulgaris. Since this time five biopsies have been performed, and all have been indicative

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Studies, observations and reports from the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, Department of Dermatology, service of Dr. M. F. Engman.

1. Chambers, R., and Grand, C. G.: (*a*) The Chemotactic Reaction of Leucocytes to Foreign Substances in Tissue Culture, J. Cell. & Comp. Physiol. **8**:1 (April) 1936; (*b*) Neoplasm Studies: II. The Effect of Injecting Starch Grains into Transplanted Tumors, Am. J. Cancer **29**:111 (Jan.) 1937.

of tuberculosis. The Wassermann and the Kahn reaction were negative, and roentgenograms of the chest were normal. Results of urinalysis and examinations of the blood were also within normal limits. Inoculation of a guinea pig showed tuberculosis.

Many therapeutic agents have been tried during the patient's attendance at the clinic, with indifferent results. Some have seemed to help for a time, but all have given only temporary relief. Many visiting dermatologists have seen the patient and offered suggestions, nearly all of which have been tried. He has been given a salt-free diet, a high vitamin diet with cod liver oil and (later) concentrated viosterol, with no benefit. Weekly injections of a gold and, later, of a bismuth preparation have been given. Irradiation from the quartz mercury vapor glow lamp and roentgen therapy were tried. After the latter the lesion became much worse. Injections of old tuberculin seemed to help more than anything for a time. This substance was injected into the lesion. An emulsion of tubercle bacillus as prepared by Mulford was used, but was of no benefit.

A, lesions of lupus vulgaris as they appeared in September 1937. *B*, lesions in August 1938, after treatment.

On Nov. 12, 1937, injections of the starch suspension were begun. The patient was given 0.1 cc. directly into one of the nodules at the edge of the lesion. Injections were made into three or four areas at a treatment. Treatments were given at intervals of one to two weeks, depending on the amount of reaction. Most of the injections were given at intervals of two weeks. The lesion showed decided improvement after these injections were started. The center became a smooth, pliable scar, and only a few nodules persisted (see illustration). This treatment did not prevent the occurrence of an occasional new nodule at the edge. No other treatment was given during this time. On many occasions 0.2 or even 0.3 cc. of the solution was injected. Redness usually developed at the site of the injection and occasionally a nodular swelling. On one occasion a painful abscess formed. This broke down and drained but promptly healed. The patient did not complain of pain from the treatment but was pleased with the result and wanted more injections.

COMMENT

In regard to chemotaxis, Chambers and Grand [1a] concluded that carbohydrates, which are slowly formed from starch in the presence of serum, are probably the effective chemicals. Several carbohydrates are also good chemotactic agents, but not as lasting an effect is produced by them as by starch.

The mechanism whereby local leukocytosis acts can only be surmised. In an excellent discussion of tuberculosis, leprosy and allied mycobacterial diseases, Long [3] stated:

> Pathogenicity is a function of the monocyte and its derivative the epithelioid cell, whatever be the animal concerned. Within wide limits it appears to be true that the animal is as resistant as his mononuclear phagocytic cells.

He was referring to these acid-fast organisms.

It has been shown by Carrel [4] that leukocytes secrete growth-promoting substances that probably produce an increase in activity of the fibroblasts. He has stated that white blood cells bring substances which adult tissues require in order to cicatrize or regenerate. He has shown that leukocytic extracts, like embryonic tissue juice, possess the power of increasing the rate of multiplication of fibroblasts.

Thus, through stimulation of the local defense forces and assistance in the reparative process, it seems that enough has been done to arrest this stubborn condition.

In this part of the United States few cases of lupus vulgaris are observed. It is hoped that some one having more cases available will be able to give this therapy a further trial.

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2. Footnote deleted on proof.

3. Long, E. R.: Tuberculosis, Leprosy and Allied Mycobacterial Diseases, Science **87**:23 (Jan. 14) 1938.

4. Carrel, A.: Leukocytic Trephones, J. A. M. A. **82**:255 (Jan. 26) 1924.

"WINTER ECZEMA OF THE ARMS"

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During the past three winters I have seen several private patients with a peculiar eruption which, as far as I have been able to ascertain, has not been previously described. The lesions were limited to the extensor surfaces of the arms and occasionally extended to the forearms and shoulders. They consisted of roughly round and circumscribed dry red scaly patches, varying in size from that of a pea to that of a dime. Itching was marked, moderate or absent and when present followed rather than preceded the appearance of the patches. In all cases the eruption appeared at the onset of cold weather, and in the majority in one or more previous winters there had been a similar eruption which had failed to respond to various types of therapy during the winter but disappeared spontaneously before summer and recurred the following fall. All the patients belonged to the middle or upper class of society. They all bathed daily and the majority twice a day. They used various types of soaps and took both shower and tub baths. On questioning, most of the patients admitted that they had neglected to dry thoroughly the outer sides of their arms after bathing. In no instance was there a personal or family history of allergy, and numerous patch tests with soaps, clothing and other possible external irritants gave negative results. I have seen this eruption in only 1 patient at the clinic and never in a child. All the patients were in the third or fourth decade of life. Although the eruption occurred in members of both sexes, it was more frequently seen in women.

The roughly circumscribed and round appearance of the lesions suggested a fungous infection, but they did not contain vesicles or clear in the centers, and microscopic examinations and cultures of the scales for fungi gave negative results in every case. Only 1 or 2 of the patients had dermatophytosis of the toes, and the course of the eruption on the arms was independent of that on the feet.

TREATMENT

After using various bland salves and antieczematous tar preparations without success, because of the clinical resemblance to a fungous eruption and in spite of the lack of laboratory evidence, I began using an

ointment originally prescribed by Deeks for mycotic infections. The formula is as follows:

Salicylic acid	10 gr. (0.65 Gm.)
Oil of eucalyptus	1 dr. (3.7 cc.)
Bismuth subnitrate	1 dr. (3.7 cc.)
Wool fat,	
Ammoniated mercury ointment, each in sufficient quantity	
To make	1 ounce (29.57 cc.)

So far, in every case I have found that daily use of this ointment, combined with less frequent bathing, use of a superfatted soap and careful drying of the affected areas, has resulted in a cure in one or two weeks. The other measures when combined with the use of some other ointment have not proved effective. In a few patients the lesions were purposely reproduced after their disappearance by stopping the use of the ointment and superfatted soap and allowing more frequent bathing without careful drying. This second eruption disappeared rapidly with the same treatment as was used for the original condition.

REPORT OF A CASE [1]

I. R., a white man aged 25, born in the United States, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 14, 1938. He presented itchy round erythematous and slightly scaly patches, varying from the size of a pea to that of a dime, on the extensor surfaces of his arms and forearms (fig. 1), of four to five months' duration. He was a baker, and his arms were exposed to dough. He perspired profusely, bathed three times a day and did not dry his arms thoroughly after bathing.

Laboratory Examination.—Microscopic examination and culture of scrapings from several patches on the arms on two occasions showed no abnormality. Urinalysis, the Wassermann test and patch tests with rye flour and a patent flour gave normal results. Histologic examination of a patch on the arm showed parakeratosis, slight acanthosis, spongiosis in some areas and edema of the upper part of the cutis, with engorged blood vessels with a perivascular round cell infiltrate (fig. 2). The histologic diagnosis was eczema.

Course.—The patient was given Deeks' ointment and a superfatted soap and instructed to bathe less often and to dry his arms thoroughly after bathing. Two days later his eruption had practically disappeared; it recurred after he stopped using the salve for a few days and disappeared again after he resumed its use. He was last seen on May 7, at which time his arms were entirely clear.

1. Although this case was the only one I have observed of involvement of a patient at a clinic and the lesions were more numerous on the forearms than in most of the other cases, I am reporting it in detail because it was the only one in which I was able to obtain a photograph and histologic examination. The history, the clinical appearance of the eruption and the response to treatment were the same as in the other cases.

SUMMARY AND CONCLUSIONS

A description is given of an eczematous eruption which has the following distinctive characteristics:

1. The round red dry scaly patches resemble a fungous eruption, but fungi are not found.

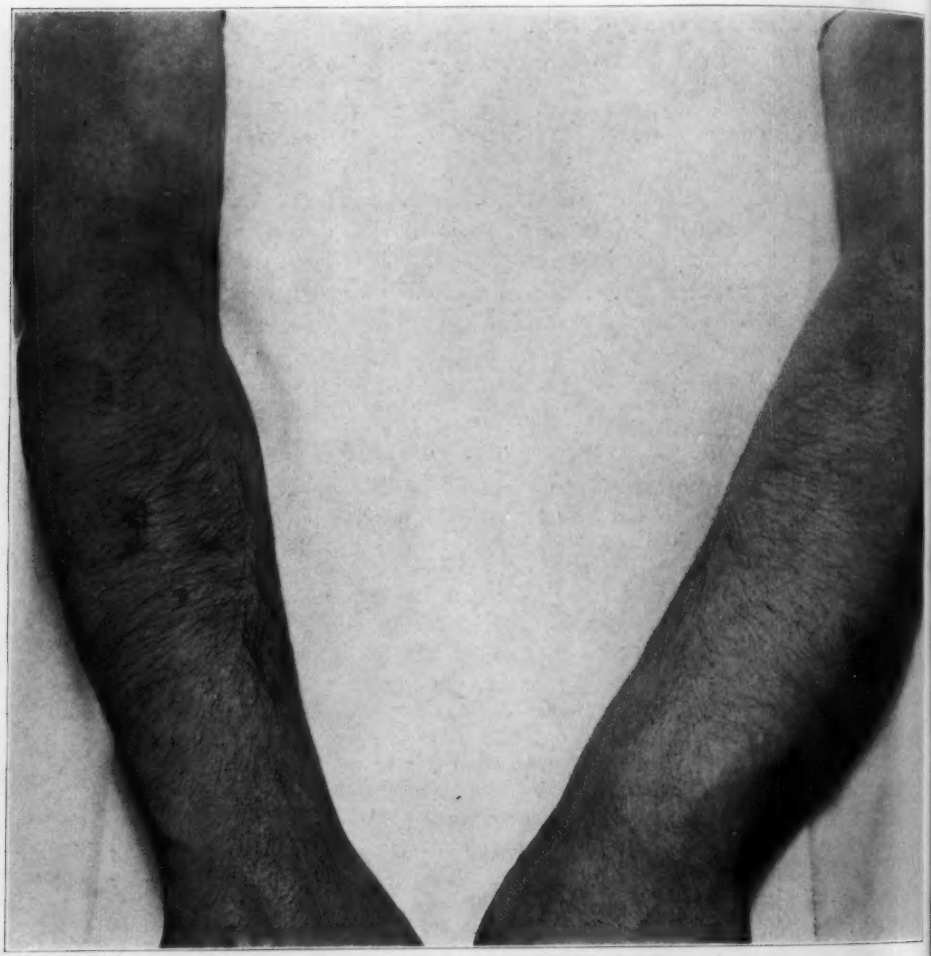

Fig. 1.—Round circumscribed erythematous scaly patches on the extensor surfaces of the arms and forearms.

2. They occur only on the extensor surfaces of the arms.

3. The eruption occurs only in the winter, disappearing spontaneously before the summer.

4. It is found only in young adults who bathe frequently without drying the outer surfaces of the arms thoroughly.

Fig. 2.—Section taken from a patch on the arm, showing parakeratosis, acanthosis, spongiosis and perivascular infiltrate in the edematous upper part of the cutis.

5. Patch tests with various possible external irritants give uniformly negative results.

6. The eruption is not influenced by antieczematous or fungicidal applications but disappears rapidly with use of Deeks' ointment and superfatted soap, less frequent bathing and careful drying of the affected areas.

Because all these six features have been noted in several cases, this eruption is considered to be a distinct and special form of eczema, for which the term "winter eczema of the arms" is suggested.

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EXTRAMAMMARY PAGET'S DISEASE AND INTRAEPIDERMAL CARCINOMA

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There is an extensive and controversial literature on the "disease of the mammary areola preceding cancer of the mammary gland" to which Paget called attention. Even more disagreement is evident concerning what has been reported as extramammary Paget's disease. Some authors have ruled out the possibility of Paget's disease occurring outside the nipple as contrary to definition, while others have cited cases of extramammary involvement as strong evidence for their conception of the disease. It appears necessary to review briefly the various definitions and conceptions of Paget's disease before reporting 3 cases on which we shall base our discussion of the subject.

Paget's disease was first conceived as a clinical entity, and little has been added to Paget's original outline of the clinical signs and symptoms. Paget [1] described the disorder as an eroded and weeping, a crusty eczematoid or a dry psoriasiform eruption of the mamilla and areola. The eruption commonly causes sensations of tingling, itching and burning. It may spread to the surrounding skin, and in all Paget's cases it became associated earlier or later with carcinoma "in the substance of the mammary gland, beneath or not far from the diseased skin, and always with a clear interval of apparently healthy tissue." To this rule exceptions have been reported, the significance of which will be discussed later. In some cases the eczema-like lesion persisted for many years without being followed by apparent tumor formation. In other instances cancer developed in the mamilla itself.

The clinical conception of Paget's disease was soon complemented and later replaced to a large degree by a histologic conception. This took place after Darier and Wickham [2] had described large round bodies in

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1. Paget, J.: St. Barth. Hosp. Rep. **10**:87, 1874.

2. Wickham, L.: Ann. de dermat. et syph. **3**:44 and 138, 1890.

the epidermis of the affected parts. The erroneous assumption that these bodies are parasites was soon corrected, but the demonstration of the large clear afibrillar "Paget cells" (pseudopsorosperms) has remained the pathognomonic feature in the histologic diagnosis of Paget's disease. In addition, there are hypertrophy and some derangement of the epidermis and a dense lymphocytic and plasmocytic infiltration of the papillary body.

There is little disagreement at the present time regarding the view that the triad of subjective symptoms, clinical and histologic signs must be present in order to justify a diagnosis of Paget's disease. Many authors, however, consider these criteria insufficient and substitute a pathogenetic conception for the clinical and histologic ones. The argument then centers around two closely connected questions: What is the nature of the Paget cell, and what is the pathogenesis of Paget's disease?

As to the nature of the pathognomonic cell, the most widely accepted views, interesting modifications of which have been offered recently by Cheatle [3] and by Fraser,[4] can be formulated briefly as follows:

1. The Paget cell is an autochthonous altered epidermal cell
   (*a*) changed regressively—degenerated, dyskeratotic;
   (*b*) changed progressively—dedifferentiated, anaplastic.
2. The Paget cell is a cancer cell originating in the mammary gland or its ducts and invading the epidermis.

The latter view, first formulated by Jacobaeus [5] in 1904, has found increasing support (Schambacher,[6] Ribbert,[7] Masson,[8] Pautrier and Levy [9] and Muir [10]). For those who accept it—and the evidence in its favor is indeed formidable—a third question arises: How does one explain so-called extramammary Paget's disease?

Several solutions are conceivable, and most of them have been offered in the literature. It seems reasonable to assume that cases of reported

3. Cheatle, G. L.: Brit. J. Surg. **11**:295, 1923.

4. Fraser, J. F.: New York State J. Med. **30**:13, 1930.

5. Jacobaeus, H. C.: Virchows Arch. f. path. Anat. **178**:124, 1904.

6. Schambacher, A.: Deutsche Ztschr. f. Chir. **80**:333, 1905.

7. Ribbert, H.: Deutsche med. Wchnschr. **31**:1218, 1905.

8. Masson, P.: Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **32**:6, 1925.

9. (*a*) Pautrier, L. M., and Levy, G.: Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **32**:19, 1925. (*b*) Pautrier, L. M.: "Paget's Disease of the Nipple.": True Cancer Tending to Invade the Epidermis and Necessitating Total and Early Amputation of the Breast, Arch. Dermat. & Syph. **17**:767 (June) 1928.

10. Muir, R.: (*a*) J. Path. & Bact. **30**:451, 1927; (*b*) Brit. J. Surg. **22**:728, 1935.

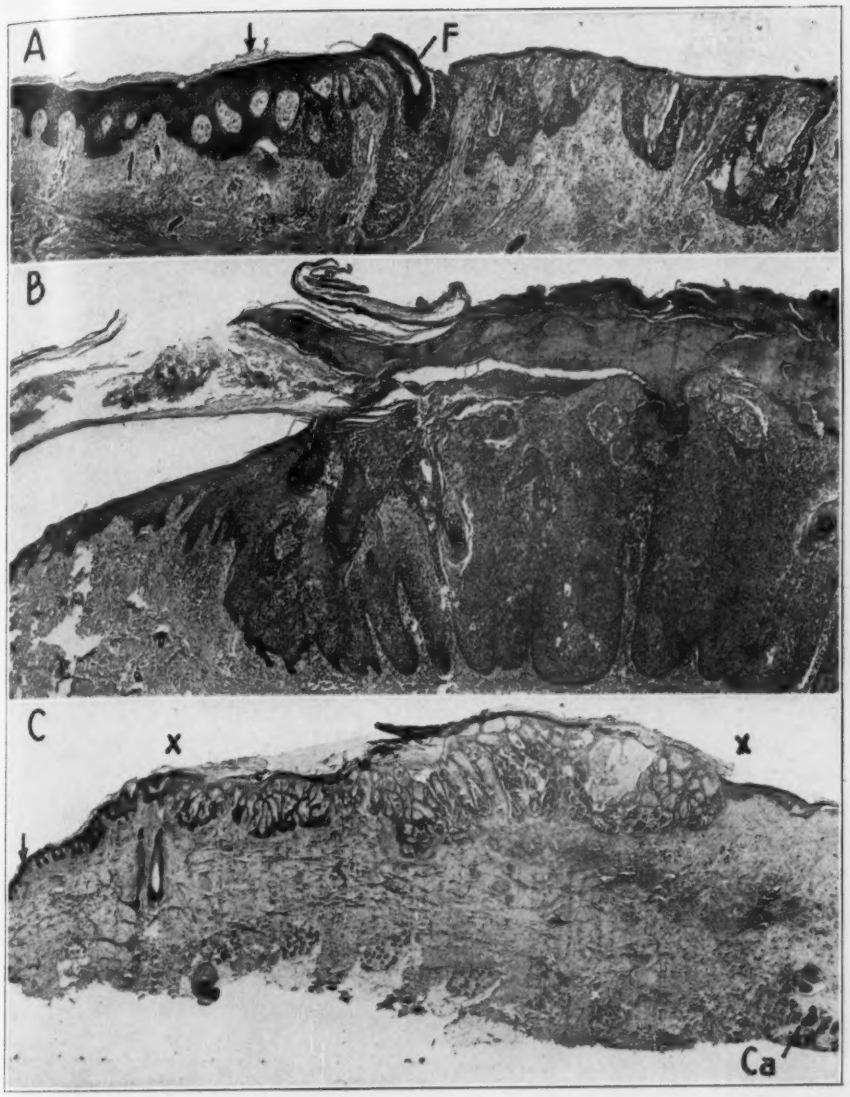

Fig. 1.— *A* (our case 1), Bowen's dermatosis (section prepared with 70 per cent alcohol, paraffin and hematoxylin and eosin) × 25. Normal epidermis appears on the left. The arrow indicates the rather abrupt start of pathologic changes in the lower half of the rete. *F* represents a hair follicle lined by normal epithelium within the altered epidermis. *B* (our case 2), intraepidermal metatypical carcinoma (section prepared with solution of formaldehyde, paraffin and hematoxylin and eosin) × 25. Normal epidermis appears on the left. Rather suddenly beginning acanthosis and replacement of the normal prickle cells by smaller undifferentiated cells can be seen, as well as horn pearls arising in the remnants of normal epidermis. *C* (our case 3), circumanal Paget's dermatosis (section prepared with 70 per cent alcohol, paraffin and hematoxylin and mucicarmine) × 9. Normal epidermis appears on the left. The arrow indicates the first intraepidermal mucin-bearing cells. *X X* indicate a zone of marked atypical proliferation of the epidermis. Relatively normal epidermis at the right contains numerous Paget cells. At *Ca* are deep nests of mucin-bearing cancer cells. Preservation of the basal layer and the reactive cellular infiltration of the corium can be seen in all 3 sections. Cutaneous appendages are present underneath the changed epidermis in *A* and *C*.

"extramammary Paget's disease" are instances of one of the following conditions:

A. Bowen's dermatosis

B. Erythroplasia of Queyrat

C. Superficial epidermoid carcinoma

D. Nevocarcinoma

E. Carcinoma of the sweat glands

F. Carcinoma of the mucous membranes bordering on the skin

Of the 70 cases which we found mentioned in the literature, only 52 were reported with sufficient detail to permit evaluation. Fifty-eight cases were reviewed in a careful critical study by Weiner,[11] and an extensive bibliography may be found in his paper.[12] We shall restrict ourselves to mentioning those cases which can be classified with reasonable accuracy.

A. BOWEN'S DERMATOSIS

The issue whether Bowen's dermatosis is a "precancerous" lesion or an "intraepidermal carcinoma" is of no consequence for the present discussion. It will satisfy our purposes to say that Bowen's disease in its typical forms consists of single or multiple lesions, which may be macular, papular or discoid and simply hyperkeratotic, warty or crusty. The lesions do not commonly cause any subjective sensations. Histologically the epidermis shows hypertrophy and a characteristic "unrest." The cells vary in size and shape; individual cells become isolated by desmolysis; clumping and giant cells occur, and mitosis may be found in all strata of the rete Malpighii. The corium always contains a certain amount of reactive infiltration.

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11. Weiner, H. A.: Am. J. Cancer **31**:373, 1937.

12. Weiner's numbering of the cases will be accepted in this paper as a matter of convenience, although we do not agree with his evaluation in every instance. References given in Weiner's paper are omitted here. The following cases mentioned in the literature are not included in Weiner's list of 58: Case 59 (glans penis): Neisser, A.: Prag. med. Wchnschr. **16**:500, 1891; Case 60 (side of breast): Rolleston, H. D., and Hunt, E. L.: Tr. Path. Soc. London **48**:211, 1897; Case 61 (mouth) and Case 62 (back): Zieler, K.: Verhandl. d. deutsch. path. Gesellsch. **17**:335, 1914; Case 63 (abdomen): Cheatle, G. L.: Brit. J. Surg. **11**:295, 1923; Case 64 (vulva): Arnd, W.: Virchows Arch. f. path. Anat. **261**:700, 1926; Case 65 (leg): Werther: Zentralbl. f. Haut- u. Geschlechtskr. **32**:679, 1928; Case 66 (buttock): Taylor, S.: Brit. J. Dermat. **42**:463, 1930; Case 67 (chest): Senear, F. E., and Caro, M. R.: A Case for Diagnosis (Extramammary Paget's Disease?), Arch. Dermat. & Syph. **23**:809 (April) 1931; Case 68 (anus): Eberts, E. M.: Internat. Clin. **4**:192, 1933; Case 69 (eyelid): Hagedoorn, A.: Brit. J. Ophth. **21**: 234, 1937, and Case 70 (popliteal space): Stout, A. P.: Am. J. Cancer **33**:196, 1938.

Large clear afibrillar cells being not infrequent in Bowen's disease, it is conceivable that the histologic features may resemble Paget's disease closely. The following description of a case of Bowen's disease will show that both clinical and microscopic classification may cause difficulties.

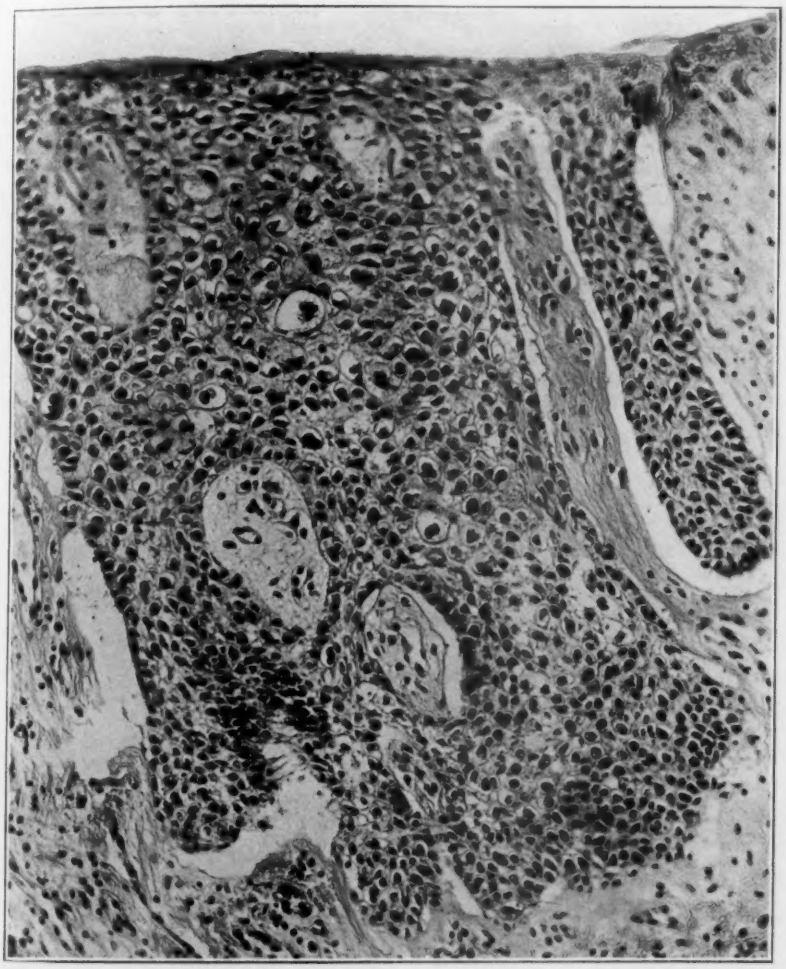

Fig. 2 (case 1).—Bowen's dermatosis (section prepared with 70 per cent alcohol and hematoxylin and eosin) × 100. Large hydropic cells are only part of the general alteration of the epidermal architecture. All the cells are large, compared with those in figure 5, which is magnified 300 times.

Our Case 1.—S. O., a white man aged 80, gave a history of rectal pain and bleeding of eight years' duration. He had been operated on for hemorrhoids in 1933, after which procedure the anal skin remained denuded. In 1933 and again in 1936

skin was grafted for "perianal excoriation." The patient received roentgen treatments in 1937.

On his admission (Dec. 23, 1937) to Eloise Hospital, a zone of partly eroded red velvety skin surrounded the anus and extended over the perineum and part of the scrotum. The lesion was moderately infiltrated, had a sharp border and exuded serous fluid. It was tender. There was a pea-sized nodular induration on the scrotum. A biopsy specimen taken from the border of the circumanal erosion showed the sections of deeply pigmented skin to be covered by slightly edematous epidermis at one end. Toward the center the relatively normal structure of the rete was replaced abruptly by highly edematous epithelial cells of unequal size and shape in irregular arrangement. Some cells appeared to be isolated from their neighbors. There were numerous mitotic figures, some multinucleated cells and cells with large hyperchromatic nuclei. The basal layer was intact, although the epidermal ridges were long and irregular. The cutaneous papillae almost reached the surface, which was covered by a crust of parakeratotic layers including dyskeratotic cells and leukocytes. Hair follicles and sweat ducts were preserved in the altered epidermis. The superficial layers of the corium showed edema, capillary dilatation and groups of lymphocytes and plasma cells. The deeper strata of the cutis were unaffected, and the cutaneous appendages were well preserved.

The patient died shortly afterward, and permission for autopsy was not obtained.

In this case the anal skin presented the clinical aspects of Paget's disease, having "a florid, intensely red, raw surface, very finely granular, as if nearly the whole thickness of the epidermis was removed . . . copious, clear, yellowish, viscid exudation" (Paget [1]). Not much could be elicited from the senile patient concerning his sensations, but the disease caused him much discomfort and the affected area was tender when touched. As for the histologic criteria, there were large hydropic cells in hypertrophic epidermis and reactive cellular infiltration in the cutis. The epidermis, however, in addition showed all the atypical cellular alterations described by Bowen,[13] and the diagnosis of Bowen's disease with secondary changes due to maceration was made.

It must be kept in mind that in Bowen's dermatosis one is dealing with an anaplastic process involving all or most of the rete cells, while the epidermis in Paget's disease shows only secondary changes due to the presence of the Paget cells. These are so isolated and different from the surrounding elements that the first observers concluded they must be parasites. This statement is made with the knowledge that later observers described intermediary forms between the normal rete cells and the Paget cells. "Intermediary forms" have frequently caused much argument in histologic discussions. The characteristic clumping cells and hyperchromatic giant cells of Bowen certainly have not been described as a part of the pathologic picture of Paget's disease of the nipple, while they have been mentioned or featured repeatedly in reports of extramammary disease.

13. Bowen, J. T.: J. Cutan. Dis. **30**:241, 1912.

It is fair to assume that such cases should be classified as instances of Bowen's dermatosis. The first case of Yoshida [14] (case 46, glans penis) and the case of Busman and Woodburne (case 53, glans penis) probably belong in this category, as do possibly the cases of Sheild, Rolleston and Hunt (case 10, pubis), Dubreuilh (case 11, vulva), Towle (case 26, back), Potter (case 30, in which the site was not specified), and Petges, Muratet and Lecoulant (case 45, vulva), the second and third cases of Yoshida [14] (cases 47 and 48, glans penis), the cases of Doerffel and Grimm (case 56, vulva) and the cases of Cheatle (case 63, abdomen), Arnd (case 64, vulva), Werther (case 65, leg), Taylor (case 66, buttock) and Senear and Caro (case 67, chest).

B. ERYTHROPLASIA OF QUEYRAT

Queyrat [15] described 4 cases of more or less dark red shiny indolent plaques on the glans penis of elderly syphilitic persons, designating the disease by the name *érythroplasie du gland*. The lesions had sharp borders and were slightly infiltrated. Biopsy of one of them showed epithelial hyperplasia and beginning carcinoma. Beck [16] mentioned this disease as possessing the following characteristic histologic changes: lengthening and broadening of the epithelial ridges, lengthening and narrowing of the papillae; absence of the stratum corneum and stratum granulosum; ovoid or spindle shape of the cells of the rete, resembling basal cells, with no marked difference in size except for some cells with giant nuclei; absence of *corps ronds,* clumping cells and grains; presence of mitotic figures in the higher strata; marked unrest of the epithelial structure, and diffuse infiltration of the subpapillary layer with lymphocytes and plasma cells. All observers have agreed that the disease is sooner or later superseded by epidermoid carcinoma. Cases of erythroplasia occurring in other parts of the body (vulva, mouth) have been reported.

There is a striking clinical resemblance between the lesions of erythroplasia, of which one of us was able to study a case in Jadassohn's clinic, and the descriptions and pictures in some of the surprisingly numerous cases reported as instances of Paget's disease of the glans penis. Of the 16 cases of penile involvement, in 9 the diagnosis was based on clinical examination only, or the data published are insufficient for evaluation: those of Paget (case 1), Tarnovsky (case 4), Sequeira (case 17), Davis (case 20), Pospeloff (case 31), Susman (case 50),

14. According to the Japanese original (Yoshida, S.: Acta dermat. **13**:702, 1929).

15. Queyrat, L.: Bull. Soc. franç. de dermat. et syph. **22**:378, 1911.

16. Beck, S. C., in Jadasasohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, pt. 3, p. 416.

DaCosta (cases 51, 52) and Neisser (case 59). The case of Tommasoli (case 6) and that of Susman (case 41) can be recognized as instances of erythroplasia with reasonable accuracy. In none of the remaining 5 cases of penile involvement, those of Pick (case 7), Yoshida (cases 46 to 48) and Busman and Woodburne (case 53), can this diagnosis be excluded definitely. It is possible that Rosenberg's case (case 19, vulva) belongs in the same group.

Erythroplasia was not mentioned in the differential diagnosis by the authors reporting any of these cases.

C. SUPERFICIAL EPIDERMOID CARCINOMA

Five cases of "extramammary Paget's disease" can be dismissed as instances of somewhat atypical ordinary epidermoid carcinoma, keratosis senilis or leukoplakia: those of Morris (case 2, neck), Ravogli (case 8, nose), Matzenauer (case 13, nose), Polland (case 27, cheek) and Glass (case 54, vulva).

In 7 cases, those of Fordyce (case 18, buttock), Towle (case 26, back), Ormsby (case 29, back), Potter (case 30, in which the site was not mentioned), Trimble (case 37, abdomen), Louste and Rabut (case 55, back) and Zieler (case 62, back), however, the lesions apparently belonged to the group variously designated as *ganz oberflächliche Rumpfhautepitheliome* (Jadassohn [17]), *carcinoide* (Arning [18]) and multiple superficial benign epithelioma (Wise [19]). The clinical resemblance of these superficial cutaneous cancers to Paget's disease gave Darier [20] reason for coining the expression "pagetoid epithelioma." This bold term emphasizes admirably both the apparent similarity and the essential difference between the two conditions, but it has led to confusion occasionally when the original sense has been forgotten.

While this type of carcinoma usually invades the most superficial parts of the corium, there are instances of intraepidermal spread, to which Jadassohn [21] first called attention. Both basal cell and prickle cell carcinoma may grow in this manner, and either type may be easily differentiated from Paget's disease if attention is paid to the cytologic characteristics: dark-staining nuclei and scanty basophilic protoplasm in basalioma and tonofibrils and keratinization in acanthoma. There is, however, one relatively small group of epidermoid carcinomas which

17. Jadassohn, J.: Beitr. z. klin. Chir. **136**:345, 1926.

18. Arning: Arch. f. Dermat. u. Syph. **138**:458, 1922.

19. Wise, F.: Multiple Superficial Benign Epithelioma of the Skin: Its Differentiation from Kindred and Similar Eruptions, Arch. Dermat. & Syph. **19**:1 (Jan.) 1929.

20. Darier, M. J.: Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **32**:1, 1925.

21. Jadassohn, J.: Dermat. Ztschr. (supp.) **26**:63, 1918.

is characterized by rather large cells without fibrils (carcinoma cubocellulare of Krompecher;[22] metatypical carcinoma of intermediary cell type of Darier and Ferrand[23]). We have had the opportunity of studying a case of intraepidermal carcinoma of this type:

TABLE 1.—*Types of Intraepidermal Carcinoma*

Type	
Dyskeratotic	Bowen's dermatosis
Prickle cell	Case of W. Jadassohn (Arch. f. Dermat. u. Syph. **171**: 412, 1935)
Basal cell	Cases of Jadassohn and others
Metatypical	
Basosquamous	Cases of Jadassohn and Montgomery
Intermediary	Our case 2
Epidermotropic	Paget's dermatosis

OUR CASE 2.[24]—M. B., a white woman aged 70, had a warty growth 2 by 1 cm. on her right thigh. The lesion had appeared several years previously and had grown slowly without causing any subjective sensations. Recently it had become eroded at one point. The entire lesion was excised, and histologic examination showed the skin to be of normal structure at both ends of the specimen. The thickness of the epidermis increased rapidly toward the center, owing to elongation of the epithelial ridges and papillae. Sharply defined groups of cuboidal cells somewhat larger than basal cells appeared in the epidermis and grew in bulk until only the basal layer and a network of normal prickle cells remained. Hair follicles and sweat ducts traversed the epidermis in normal fashion. The pathologic cells were of rather uniform size, the nuclei being round or ovoid and containing a moderate amount of chromatin and one or two nucleoli. Mitotic figures were numerous in all strata. The protoplasm appeared to be of delicate structure and vacuolated and was entirely devoid of tonofibrils, although the cells were connected with each other and with the surrounding prickle cells by intracellular bridges. While most of the cells were gathered into smaller and larger groups, a number of them were isolated among the normal rete cells. These elements became highly edematous and reached as much as two or three times the size of the neighboring cells. The pathologic cells did not form normal keratin, although an occasional cell contained granules of keratohyalin, but they shrank down to acidophilic masses in which the nuclei sometimes remained visible. Isolated cells which had undergone this process closely resembled the "grains" of Darier. The subpapillary layer of the corium contained wide capillary vessels and a rather diffuse moderately dense infiltration of lymphocytes and plasma cells.

This case, while the clinical picture did not resemble Paget's disease, had some of its histologic features. The epidermis was hypertrophic and contained large afibrillar cells singly and in groups. There was also the reactive cellular infiltration of the corium. The essential difference was not so much the formation of compact masses by the pathologic cells as the fact that even the individual cells remained in close connec-

22. Krompecher, E.: Beitr. z. path. Anat. u. z. allg. Path. **28**:1, 1900.

23. Darier, M. J., and Ferrand, M.: Ann. de dermat. et syph. **3**:385, 1922.

24. Dr. Louis J. Bailey, of Eloise Hospital, supplied the clinical data and the specimen. This case was presented before the Dermatological Section of the Michigan State Medical Society (Pinkus, H.: J. Michigan M. Soc. **37**:533, 1938).

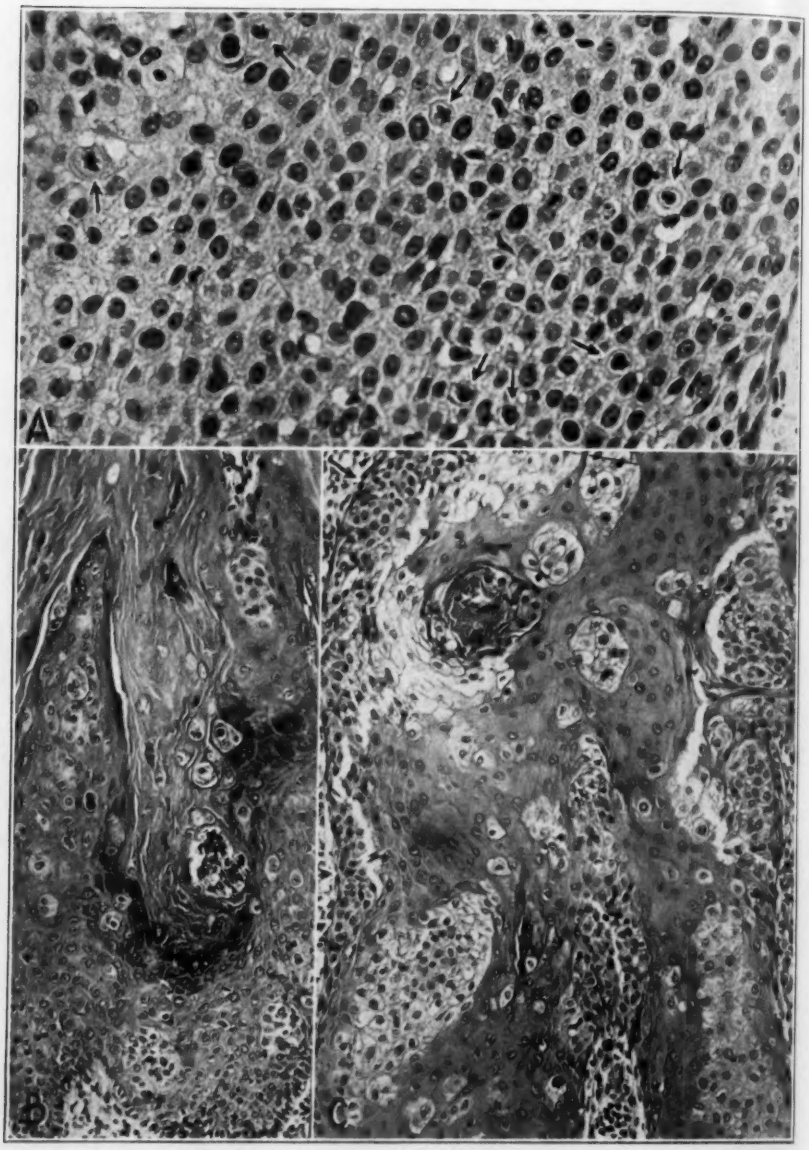

Fig. 3 (case 2).—Intraepidermal epidermoid carcinoma (section prepared with solution of formaldehyde and hematoxylin and eosin). In *A* (× 350) uniform, more or less cuboid cells can be seen connected by intercellular bridges. Arrows point to some of the numerous mitoses. In *B* and *C* (× 125) larger and smaller nests and isolated "clear cells" are present within the epidermis. The basal layer is preserved. Hypertrophy of isolated cancer cells can be seen in the rete; these form "grains" in the horny layer. Malignant cells are sharply differentiated from, but in protoplasmatic connection with, the normal prickle cells.

tion with the surrounding prickle cells. Tonofibrils were absent, but protoplasmatic bridges could be demonstrated between the malignant and the normal cells, indicating a much closer relationship of the two cell types than the one existing between the Paget cell and its surroundings. On the other hand, no transitional links existed between normal and anaplastic cells. The latter were set in the epidermis in the manner typical of intraepidermal malignant growths. No extraepidermal source of cancerous cells being obvious, we believe that this lesion was intraepidermal epidermoid carcinoma of intermediary cell (Darier) type.

This case exemplifies the possibility that this type of carcinoma may closely approach the histologic and perhaps some of the clinical features of Paget's disease.

D. NEVOCARCINOMA

The view that Paget's disease of the nipple may arise in the epidermal melanoblasts of this region has been expressed by Audry,[25] Kreibich [26] and Zieler.[27] Hartzell reported a case (case 23) in which the clinical and histologic features were those of Paget's disease; the condition started from a pigmented nevus on the forearm. Civatte described a case of Paget's disease of the axilla (case 43) in which he found a deep carcinoma of the sweat glands and a superficial nevocarcinoma. Miescher presented a case (case 44) of involvement of the vulva in which he could not decide between the diagnosis of Paget's disease and that of melanocarcinoma. Recently Stout reported a case (case 70, popliteal space) in which a cutaneous lesion resembling Paget's disease clinically and histologically was followed by metastasis to the femoral lymph nodes. The metastatic tumor had the characteristics of a malignant amelanotic melanoma.

Audry, Civatte and Miescher apparently used the prefixes "nevo-" and "melano-" in order to describe a carcinoma composed of large undifferentiated cells. Lack of differentiation having been mentioned often as characterizing Paget's carcinoma, these cases may possibly be explained on a different basis (see the succeeding section, E). Kreibich's deductions appear to be highly hypothetic and based on insufficient evidence. Hartzell's, Stout's and Zieler's cases, however, appear to be true instances of melanotic tumor. The lesion in Zieler's case [28] started on the left mamilla and within nine years spread as a pruritic psoriasiform eruption over the left side of the chest. The patient died at the age of 71 years without development of carcinoma of the breast. The "Paget cells" in this case contained melanin; according to a later

25. Audry, C.: Ann. de dermat. et syph. **7**:529, 1906.
26. Kreibich, C.: Berl. klin. Wchnschr. **48**:1293, 1911.
27. Zieler, K.: Verhandl. d. deutsch. path. Gesellsch. **17**:335, 1914.
28. Zieler, K.: Virchows Arch. f. path. Anat. **177**:293, 1904.

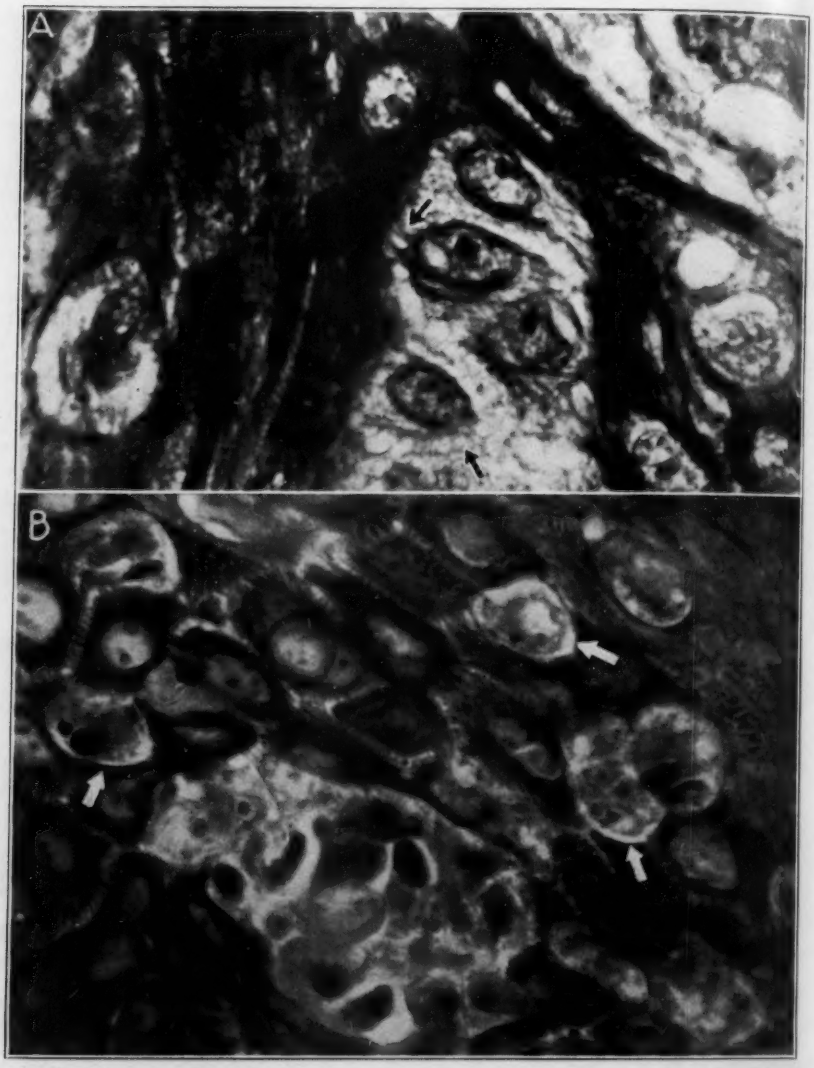

Fig. 4.—*A* (case 2), a section prepared with solution of formaldehyde and Unna's alum-methylrosaniline-iodine stain for tonofibrils; × 1,050. Small groups and individual cancer cells are surrounded by normal prickle cells. The malignant cells are light because of the absence of dark-staining tonofibrils. Arrows point to some of the intercellular bridges that connect the "afibrillar" cells with each other and with normal cells. *B* (case 3), a section prepared with Kolster's fluid and Unna's water blue-orcein-eosin-safranin stain for tonofibrils; × 1,050. Small groups and individual cancer cells are surrounded by normal prickle cells. The malignant cells contain no tonofibrils and are not in protoplasmatic connection with the normal cells. Arrows point to clear intercellular spaces. Some of the Paget cells contain blue-staining amorphous masses (mucin).

publication,[27] the lesion was a typical melanoma spreading intraepidermally. The cases of Satani (case 36, axilla), Werther (case 65, leg) and Taylor (case 66, buttock) possibly belong in this group (Stout).

E. CARCINOMA OF THE SWEAT GLANDS

Sekiguchi [29] was probably the first author to suggest that extramammary Paget's disease arises from the sudoriferous ducts. The same view was elaborated later by Pautrier [30] and Crosti.[31] Recently Weiner [11] described a case of carcinoma of the apocrine glands of the vulva offering all the features of Paget's disease. He collected 25 cases in which the same pathogenesis was likely or at least possible, the involvement in all of them occurring in regions where apocrine glands are found normally.

In our opinion, the diagnosis appears acceptable in the following 9 cases: those of Crocker (case 3, scrotum and penis), Holzknecht (case 12, axilla), Jungmann and Pollitzer (case 14, axilla), Zieler (case 16, axilla), Sekiguchi (case 34, scrotum), Satani (case 36, axilla), van der Hoop, Bonne and Wassink (case 40, vulva), Civatte (case 43, axilla) and Weiner (case 58, vulva). Twelve other cases may fall into the same category: those of Darier and Couillaud (case 5, anus and scrotum), Sheild, Rolleston and Hunt (case 10, penis and scrotum), Dubreuilh (case 11, vulva), Rosenberg (case 19, vulva), Arzt and Kren (case 39, vulva), Tashiro (case 42, vulva), Miescher (case 44, vulva), Petges, Muratet and Lecoulant (case 45, vulva), Drake and Whitfield (case 49, vulva), Doerffel and Grimm (case 56, vulva), Noguer-More (case 57, scrotum) and Arnd (case 64, vulva).

F. CARCINOMA OF THE MUCOUS MEMBRANES BORDERING ON THE SKIN

The following case was observed at Eloise Hospital:

Our Case 3.—A. A., a Negro aged 57, had had draining buboes in 1910 and a chancre in 1918, for which he received antisyphilitic treatment. He complained of pruritus ani of two years' duration. Two months after the onset of symptoms he began to pass blood in his stools. He had also noticed enlargement of the inguinal lymph nodes during the preceding eighteen months, and for more than a year he had had increasing difficulty in passing his stool. He had been variously treated for anal fissures and rectal stricture, supposedly due to lymphogranuloma venereum. An examination in February 1937 had shown loss of pigment, reddening, erosion and fissuring of the skin around the anus and a few anal tags. There had been tenderness and spasm of the anal sphincter, but proctoscopic examination revealed only an easily bleeding rectal mucosa. The inguinal nodes on the left were enlarged and tender, but not fluctuant. The Frei test was positive.

29. Sekiguchi, S.: Ann. Surg. **65**:175, 1917.
30. Pautrier, L. M.; Levy, G., and Diss, A.: Presse méd. **35**:1041, 1927.
31. Crosti, A.: Gior. ital. di dermat. e sif. **73**:1021, 1932.

Examination in February 1938 showed a slightly emaciated man. He had multiple large matted wooden-hard lymph nodes in both groins. The skin over a radius of 2.5 cm. around the anus had a bright red velvety surface that looked as if the rectal mucosa had grown over it. Small whitish islands were present within the red area. The lesion had sharp borders, was slightly indurated and elevated and exuded serous fluid. It was intensely pruritic and was painful when touched. The anus itself was indurated, fissured and so narrow that it did not admit the finger. The Kline exclusion test of the blood was negative.

Histologic Examination.—Biopsy specimens taken (*a*) from the border of the circumanal lesion, (*b*) from the region of the anoepidermal junction and (*c*) from the inguinal lymph nodes showed:

(*a*) The sections of skin from the border of the circumanal lesion were covered by epidermis throughout and contained normal hair follicles and glands. The epidermis, which was normal and rather deeply pigmented at one end of the specimen, soon became increasingly hypertrophic and contained in all its strata single light-staining afibrillar cells, more numerous in the deeper layers. These cells were from one to three times the size of prickle cells, were round or ovoid and were not in protoplasmatic connection with their neighbors. Their nuclei were fairly rich in chromatin, round or compressed by some light-staining material that filled the greater part of the larger cells. Numerous mitotic figures were present. The cells retained their round shape in the upper layers of the rete and in the stratum corneum, where they shrank to small round bodies with pyknotic or fading nuclei. Similar cells were present between the lining epithelium of some hair follicles and sweat ducts.

In the middle of the length of the sections there was marked atypical proliferation of the epidermal ridges, which formed a complicated network. In routine specimens (fixed in 70 per cent alcohol) the epidermis appeared to be transformed into a system of hollow tubes lined by the basal layer and containing a mixed suspension of the round cells and distorted prickle cells. Sections fixed in Kolster's fluid[31a] for mitochondria and tonofibril staining, however, showed that this aspect was due only to shrinkage of the edematous tissues. The epidermis was really solid and compact, the pathologic cells being in the majority. The surface of these parts was covered by a crust composed of horny lamellae, serum and degenerating cells. Toward the other end of the sections the epidermis resumed its more nearly normal shape, but contained a great number of single clear cells or small groups, mainly in the lower strata. At this end of the specimen, more than 1 cm. remote from the border of the lesion, several large nests of epithelial cells were present in the deep parts of the cutis, and smaller groups of similar cells could be seen in the lymph spaces situated more superficially, but not in the immediate vicinity of the epidermis. These cells were round or polygonal and varied in size. The smaller ones had a large round, rather dark nucleus and a slightly basophilic protoplasm. The larger elements had a paranuclear light zone which compressed the nucleus, while the largest forms were of typical signet shape. Mitotic division was fairly frequent. The cutis in addition contained foci of lymphocytes and plasma cells near the cancerous infiltration and in the subpapillary layer bordering the clear cells.

Staining with mucicarmine showed that many of the cancer cells in the cutis, as well as all strata of the epidermis, contained mucin.

31a. Kolster's fluid has the following composition: 5 per cent solution of potassium dichromate, 40 per cent; 2 per cent solution of chromalum, 40 per cent; solution of formaldehyde, 20 per cent.

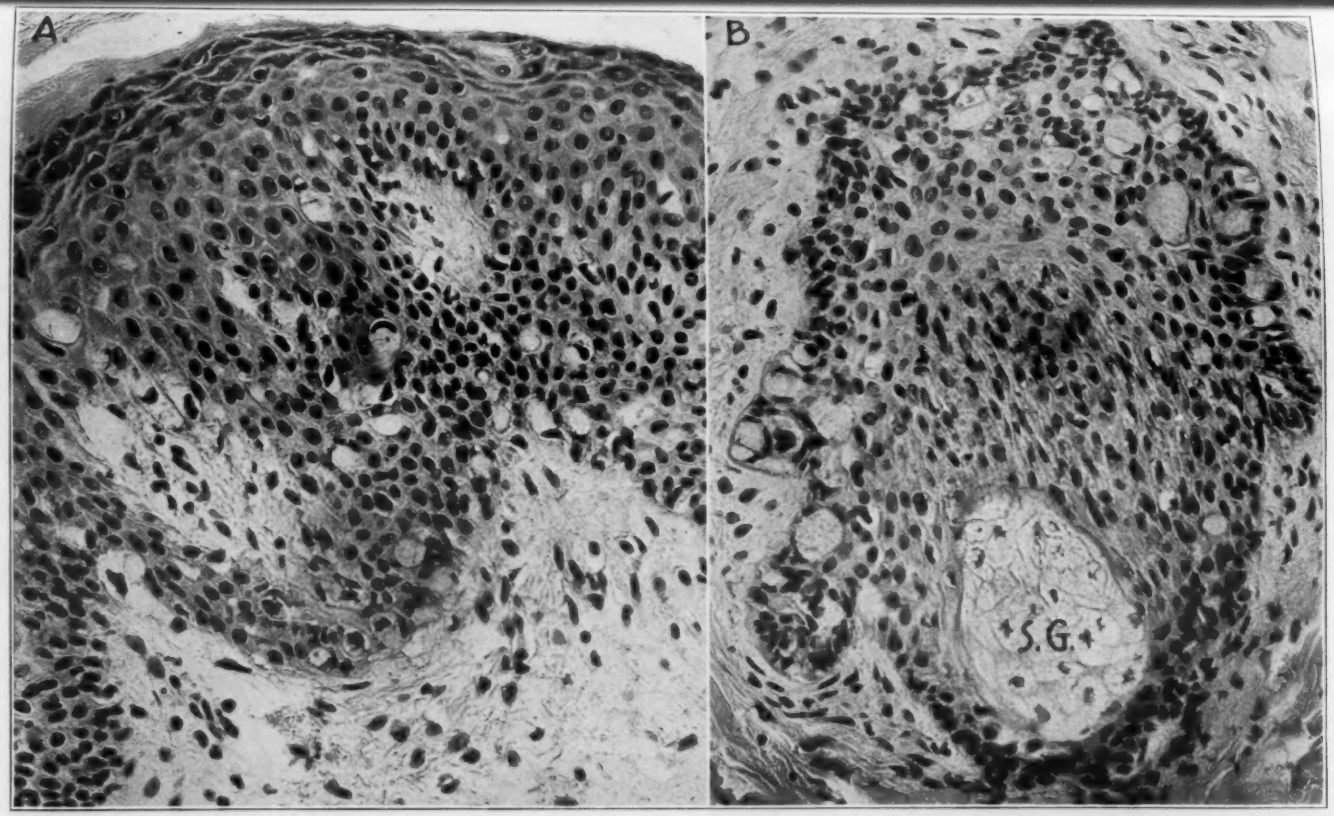

Fig. 5 (case 3).—Epidermotropic rectal carcinoma (section prepared with solution of formaldehyde and hematoxylin and mucicarmine) × 300. At *A*, the epidermis has normal structure except for the intercalation of single afibrillar cells, many of which have signet shape and contain mucicarminophilic material. At *B*, mucin-bearing cells are present in the epithelial lining of a hair follicle. *S. G.* designates sebaceous gland cells.

(*b*) Sections from the anal mucocutaneous junction showed extensive cancerous growth, of similar type to that in sections from location (*a*), invading the connective tissue, while the lining of stratified squamous epithelium contained numerous mucin-bearing cells.

(*c*) The inguinal lymph node was largely replaced by neoplastic epithelial growth. The cells formed compact nests, or strands of two or three rows of cells. There was a suggestion of alveolar structure in some places. Most of the cells were cuboidal, but a number of larger elements, some of which were signet shaped, were present. Mucin could be demonstrated in about 10 to 30 per cent of the cells. There was no evidence of keratinization.

Course.—Roentgen treatment to the anal and the inguinal region produced some improvement, but severe pruritus persisted. Two months later several pea-sized nodules appeared in the skin of the perineum at some distance from the circumanal lesion. Excision of one of these nodules showed invasion of the middle layers of the corium by carcinoma of the type found in the lymph nodes. The papillary body and the epidermis were not affected. The general condition of the patient improved temporarily after colostomy, but lymphedema of the legs and genitalia developed, and he died of cachexia Aug. 20, 1938.

Autopsy.—At autopsy there was an obstructing annular infiltrating carcinoma of the rectum 8 cm. above the anal orifice. There were metastases to the lungs, the left parietal pleura, the liver, the omentum, the peritoneum, the mucosa of the bladder, the skin of the scrotum and the tracheal, bronchial, pyloric, left adrenal, anterior aortic and bilateral iliac, sacral and inguinal lymph nodes.

The microscopic structure of the primary tumor and its metastases varied a great deal. While growth in cords of cuboidal cells was most common, there were differentiation into high columnar cells and definite acinar arrangement in some parts and lymphatic spread of groups of large mucin-laden cells in others. Figure 6 illustrates a few of these variations.

The final diagnosis from the dermatologist's point of view was "extramammary Paget's disease," on the basis of an infiltrating carcinoma of the rectum with mucin-bearing cells which had grown by direct extension in the lymph spaces of the anal mucosa and of the circumanal skin, in the stratified epithelium of the anus and in the circumanal epidermis and which had produced widespread lymphatic and hematogenous metastases in numerous organs.

The analogy between the lesion on the nipple plus underlying mammary carcinoma of classic Paget's disease and the circumanal disease plus rectal carcinoma in this case appears to be perfect. The pruritic, inflammatory-looking eruption, the foreign cells in the hypertrophic epidermis, the dense cellular infiltration in the corium and the cancer of the lining epithelium of an organ opening on this skin were present. Apparent differences, such as the relatively short interval from the onset of subjective symptoms to the occurrence of metastasis and the relatively small size of the "Paget cells," will be discussed later.

Cases of similar involvement were described by Arzt and Kren (case 32, anus and perineum [32]) and Eberts (case 68, anus). Dunn [33]

32. The case was originally presented by O. Kren (Wien. klin. Rundschau **28**: 59, 1914) and later described as case 10 by L. Arzt and O. Kren: (Arch. f. Dermat. u. Syph. **148**:284, 1924).

33. Dunn, J. S.: J. Path. & Bact. **33**:297, 1930.

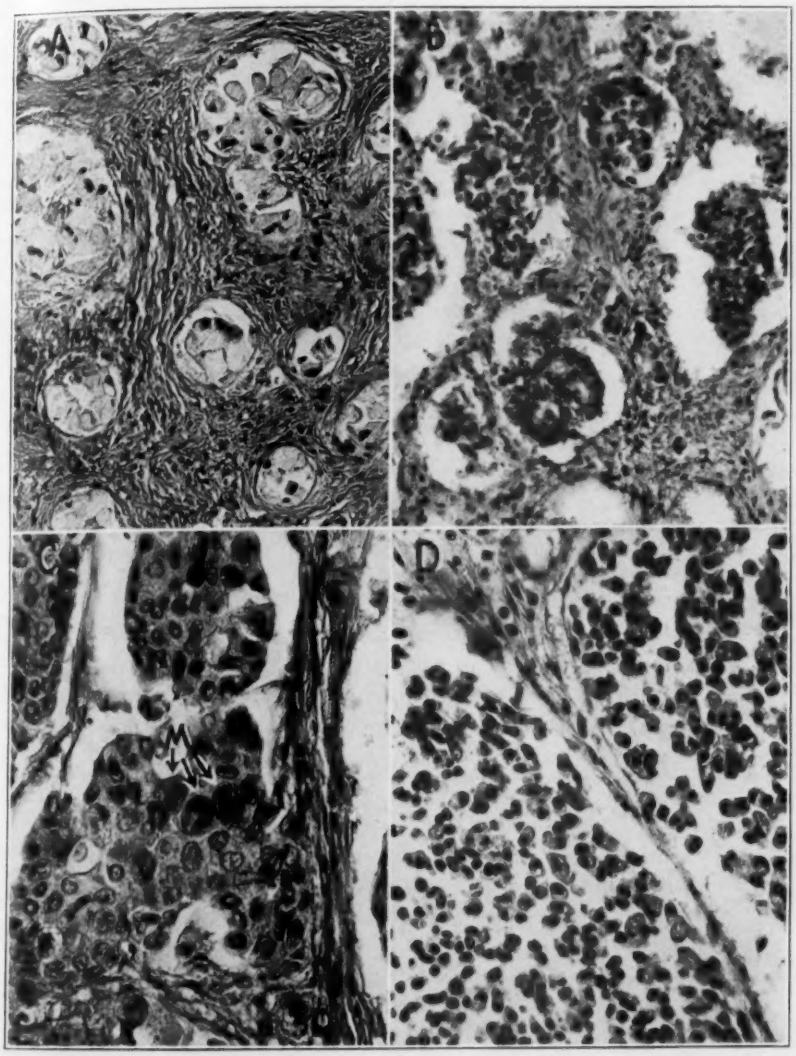

Fig. 6 (case 3).—Carcinoma of the rectum and metastases. *A*, groups of large mucin-laden cells infiltrating the rectal wall (section prepared with solution of formaldehyde and hematoxylin and eosin) × 150. *B*, alveolar arrangement of tumor cells in metastasis to the lung (solution of formaldehyde and hematoxylin and eosin) × 150. *C*, cords of cuboidal cells in metastasis to inguinal lymph nodes (solution of formaldehyde and hematoxylin and mucicarmine) × 300. *M* designates a group of mucin-bearing cells. *D*, detail of cancer cells in the cutis corresponding to figure 1, *C* (*Ca*) (70 per cent alcohol and hematoxylin and mucicarmine) × 300. Mucin-bearing cells are present without definite arrangement.

reported a case of intraepidermal spread of a rectal carcinoma, presumably without the clinical features of Paget's disease. Perhaps the old case of Darier and Couillaud (case 5, anus and scrotum) falls into this category. Interesting in this connection is Fox and Macleod's case (case 15, umbilicus), in which remnants of Meckel's diverticulum were found in the center of a lesion bearing all the features of Paget's disease. No carcinoma was found, but only part of the tissue was examined microscopically.

COMMENT

This survey of "extramammary Paget's disease" shows that the cases reported under this heading can be divided into two groups. The first group comprises cases in which the lesions bear only a more or less superficial resemblance to Paget's disease of the nipple and are really instances of such conditions as Bowen's dermatosis, erythroplasia or

TABLE 2.—*Classification of Cases of "Extramammary Paget's Disease"*

Diagnosis	Reasonably Assured	Possible
Bowen's disease	2	13
Erythroplasia	2	6
Superficial epithelioma	4	3
Nevocarcinoma	2	3
Carcinoma of sweat glands	9	12
Carcinoma of sebaceous glands	..	2
Carcinoma of mucous membrane	3	2
Ordinary epidermoid carcinoma	5	..
Unclassifiable	18	..
Paget's disease of bones	1	..

superficial epidermoid carcinoma of other types. The second group consists of those in which the lesions by clinical and histologic criteria closely resemble the classic picture and are constantly associated with some kind of extraepidermal carcinoma, be it a melanoblastoma (Masson's theory), cancer of the sweat glands or carcinoma of the bowel. We may now attempt to answer the three questions raised at the beginning of this paper: 1. What is the nature of the Paget cell? 2. What is the pathogenesis of Paget's disease of the nipple? 3. Is there true extramammary Paget's disease?

Nature of the Paget Cell.—The mucin content of both cancer and intraepidermal cells in our case 3 leaves no doubt that the "clear cells" in this case were of extraepidermal origin—were rectal cancer cells. The cases of Dunn and Eberts, who reported exactly the same observations, show that this phenomenon is not singular. Such cases, as Muir and Pautrier have pointed out, add considerably to the strength of the theory that the Paget cells of the areolar disease are cancer cells of extraepidermal origin, even though a specific cellular product has not

been demonstrated. Arnd [34] showed that the classic Paget cells are not edematous and hydropic, but are full of glycogen. From this he concluded that the cells are probably not of mammary origin, as the normal mammary gland does not contain glycogen (Gierke [35]). Mammary carcinoma, however, may contain this substance (Lubarsch,[36] Gierke [37]), and Arnd himself conceded that the Paget cells may arise in the large milk ducts.

The fact, however, that the presence of so important a cellular product as glycogen was discovered more than thirty-five years after the first description of the characteristic cells indicates that the use of refined cytologic methods instead of the routine histologic procedures is apt to add more evidence pro or contra.[38] At the present time the accumulated evidence of cases of areolar and so-called extramammary Paget's disease favors the view that the Paget cell of the lesion on the nipple is the malignant cell of a ductal cancer.

Pathogenesis of Paget's Disease of the Nipple.—Against this view the argument has been advanced that migration of cancer cells in the epidermis for any considerable distance cannot be imagined, and that the finding of isolated and widely scattered Paget cells is proof of their origin in loco. Another argument raised against the extraepidermal origin of these cells is that the disruption and displacement of the cells of the basal strata by foreign elements would obstruct the formation of a normal rete and horny layer.

Observations like those in our case 3 disprove both these arguments. There can be no doubt that at least the cells in the border of the lesion traveled there by intraepidermal routes, the nearest point at which carcinoma was present in the corium being more than 1 cm. distant. It may also be seen that in spite of the extensive replacement of the rete and even of its basal layer by tumor cells the general architecture of the epidermis was fairly well preserved.

The light shed on the biology of cancer and of epidermis by tissue culture makes it much easier to understand the mechanics of such observations. Explantation has demonstrated the ameboid motility of cancer cells, as well as the cells of most other tissues, including the epidermis. Culture of human epidermis in particular has shown a surprisingly great capacity of individualization among the basal cells

34. Arnd, W.: Virchows Arch. f. path. Anat. **261**:700, 1926.

35. Gierke, E.: Beitr. z. path. Anat. u. z. allg. Path. **37**:502, 1905.

36. Lubarsch, O.: Virchows Arch. f. path. Anat. **183**:188, 1906.

37. Gierke, E.: Ergebn. d. allg. Path. u. path. Anat. **11**:871, 1907.

38. Cheatle and Cutler asserted that Ludford studied a case of Paget's disease of the nipple by cytologic methods. We were unable to locate any publication of his results.

and great plasticity of the entire architecture of the epidermis, including the system of tonofibrils (Pinkus [39]).

From the purely mechanical point of view the histologic picture of Paget's disease can be easily explained by the migration and multiplication of foreign cancer cells in the epidermis. The difficult problem is a biologic one. The epidermis usually either succumbs to the invasion of foreign cells, inflammatory or malignant, or rids itself of such elements by shedding them onto the surface. In Paget's disease, however, cancer cells and epidermis remain in biologic balance for a long time. Neither side gets the upper hand, although the symbiosis is certainly not perfect. The parasitic cells cause some irritation and alteration of the host tissue, which is evident in the proliferation of the epidermis, the degeneration of some of its cells and the cellular reaction of the corium. Further evidence of this irritation may be seen in the symptoms and signs of inflammation which constitute the clinical picture of Paget's disease.

We can only guess at the causes of this peculiar symbiosis. They must be sought in certain qualities of either host or guest cells, perhaps of both. While there is no indication that the epidermis of the bearer of Paget's disease is different from that of other persons, it has been noted by one of the earliest observers (Thin [40]) that the Paget carcinoma is of a peculiar type when it leads to tumor formation and metastasis. This so-called ductal cancer often is made up of rather undifferentiated cuboidal or spheroid cells forming amorphous masses rather than "adenomatous" structures and thus shows low histogenic qualities, a fact that has added to the confusion concerning the site of origin of the tumor. Tumor formation and metastasis usually occur late, after intraductal cancer and intraepidermal spread have been present for a long time (epidermotropic carcinoma, Masson [8]). Even at a time when tumor formation and metastasis have developed in the breast, there is often no invasion of the cutis from the intraepidermal cancer. This has been another argument in favor of the thesis that the cutaneous lesion is different from the deep carcinoma. Again tissue culture has shown that strains of cells of different biologic quality can be isolated from one malignant tumor in a human being (Pinkus [41]).

It is this quality of epidermotropism, plus the resulting symbiosis of cancer and epidermis, that is the most significant aspect of Paget's disease of the nipple. In comparison with it the question of the exact ways and means by which the cancer cells reach the epidermis loses some of its importance. Muir [10b] has shown that in most cases the

39. Pinkus, H.: Arch. f. Dermat. u. Syph. **165**:53, 1932.
40. Thin, G.: Brit. M. J. **1**:760 and 798, 1881.
41. Pinkus, H.: Am. J. Cancer **29**:25, 1936.

cells spread by strictly intraepithelial routes through the openings of the milk ducts, but it does not appear justifiable to make this fact the main criterion for a diagnosis of Paget's disease. In at least 2 cases on record (Rolleston and Hunt, case 60; Kyrle [42]) the cancer cells reached the epidermis by routes other than the openings of the ducts and produced the clinically and histologically typical picture of Paget's disease.

We agree with Muir that the mere presence of mammary cancer cells in the epidermis does not justify a diagnosis of Paget's disease. For this diagnosis it is necessary to have evidence of the spread of the malignant cells in the plane of the epidermis—that is, laterally from the site of entry. It is clear that this evidence cannot always be gleaned from a chance section of a small biopsy specimen. At any rate, it is not for the pathologist alone or for the clinician alone to make a definite diagnosis of Paget's disease. Paget's disease of the nipple should be diagnosed only in the presence of symptoms and clinical and pathologic signs of the unique biologic process of symbiosis of the epidermal cells and of cancer cells of extraepidermal origin.

A biologic conception of Paget's disease and its pathogenesis like the one just sketched fulfils two requirements: 1. It permits one clearly to differentiate Paget's "disease of the mammary areola" from similar dermatoses on the basis of a few criteria that can be established with relative ease. 2. It is broad enough to comprise the whole range of variations that Paget's disease may show as regards the extent of the lesion and the relation in time between cutaneous disease and carcinoma. A lesion such as the small weeping spot found by Sekiguchi [29] on the mamilla in a case of "bleeding nipple" due to ductal cancer, and the large eczematous lesion that spreads over large parts of the chest within many years without tumor formation but with subclinical carcinoma somewhere in the breast both fulfil the criteria. The argument concerning the exact site of origin of the cancer, whether in the ductal ostiums,[43] the excretory ducts, the lactiferous sinuses, the milk ducts of any order or even the secretory acini, loses its theoretic significance, although certain types of malignant change apparently give rise to the Paget cutaneous lesion much more frequently than others.

Extramammary Paget's Disease.—It is evident that the conception of Paget's disease of the nipple as a more or less well balanced symbiosis between the epidermal cells and parasitic cancer cells of extraepidermal

42. Kyrle, J.: Arch. f. Dermat. u. Syph. **83**:187, 1906.

43. The ductal ostiums are a biologic part of the glandular system and have properties different from the epidermis in which they are embedded, if a conclusion by analogy of the relationship of the sweat ducts and epidermis is permitted. The evidence for this view is to be published elsewhere.

origin not only permits but requires the inclusion of some cases of "extramammary" involvement. As a matter of fact, a sharp differentiation between mammary and extramammary disease is virtually impossible because cases of borderline involvement exist. In Rolleston and Hunt's case Paget's disease following a mammary abscess (case 60) started around the sinus tract and involved the nipple only secondarily, thus being "extra-areolar" on the basis of a carcinoma of the breast. The case of Grynfellt, Margarot and Guibert,[44] in which the milk ducts were free but cancer of the sweats ducts was found, is an instance of Paget's disease of the nipple on an "extramammary" basis.

There is no reason to exclude cases in which carcinoma of the apocrine glands in other parts of the body was causative (group E). (The terminology will be discussed later.) No cases are on record of involvement attributable to cancer of the other cutaneous appendages (eccrine or sebaceous glands), with the possible exception of Sheild, Rolleston and Hunt's case (case 10, pubis), in which the observers attributed the condition to cancer of the sebaceous glands, and Hagedoorn's case (case 67, eyelid), in which a meibomian gland was found affected. The description and photographs in the latter case, however, do not appear convincing enough to justify a definite diagnosis of "extramammary Paget's disease."

From a biologic point of view there is no reason to exclude cases in which the disease was based on cancer of a mucous membrane (group F), in spite of minor histologic differences, like the relatively small size of the intraepidermal cells in our case. The boundary is clearly given in the requirement that both clinical and histologic criteria must be fulfilled for a diagnosis of "extramammary Paget's disease." This postulate is not arbitrary. The clinical criteria of itching and inflammation indicate the extraneous quality of the intruding cells and apparently are not duplicated by new growths of epidermal origin.

The much cited case of Borst[45] (prickle cell carcinoma of the lip with intraepidermal extension) and a case of apparently similar involvement reported by Zieler (case 61, mouth) are thus excluded, as well as all cases of intraepidermal epidermoid carcinoma (groups A, B and C). It remains to consider nevocarcinoma (group D). The cases of Hartzell, Zieler and Stout no doubt presented the clinical features of Paget's disease. If one accepts Masson's theory of the extraepidermal origin of the nevus cell, these cases fulfil all the criteria. Even as a supporter of the epidermal derivation of the melanoblast one can argue

44. Grynfellt, E.; Margarot, J., and Guibert, H. J.: Bull. Assoc. franç. p. l'étude du cancer **21**:348, 1932.

45. Borst, M.: Zentralbl. f. allg. Path. u. path. Anat. **15**:541, 1904.

that the nevus cell has become so different that it may act as a foreign element in the epidermis. Further observations, however, appear to be necessary before the position of nevocarcinoma can be ascertained.

CONCLUSIONS

We have tried to show that in certain cases reported as instances of "extramammary Paget's disease" the condition presents a close clinical, histologic and biologic resemblance to Paget's disease of the nipple.

The question has been asked whether one has a right to affix Paget's name to conditions of this type or whether the name should be restricted to the lesion of the nipple. We prefer to take the former stand, for several reasons. Paget [1] himself visualized the possibility of the characteristic combination of an inflammatory-looking cutaneous lesion and deep cancer occurring in other parts of the body. Moreover, the conception of Paget's disease has changed considerably from the original clinical concept. In particular, Paget's name has been used without objection for the pathognomonic cell, which he did not describe. One may doubt the advisability of the frequent use of authors' names in medicine, but with respect to Paget's disease, the name has become so generally used that the descriptive terms dermatitis papillaris maligna (Thin [40]) and dermatitis epithelialis degenerativa (Lang [46]) are practically forgotten.

We propose to go a step further and to affix Paget's name to the biologic phenomenon of which the disease described by him is the best known and the most frequently observed example: the phenomenon of more or less well balanced symbiosis of the epidermal cells and a strain of foreign cancer cells. We propose to use the designation "Paget's disease," or better "Paget's dermatosis" (in distinction from Paget's disease of the bones), in all cases in which the Paget phenomenon is demonstrable. The use of this designation should have a great practical advantage. It would remind one to look for deep carcinoma and not to lose time in treating the cutaneous lesion as precancerous or as superficial epidermoid carcinoma.

SUMMARY

A discussion is given of the nature and pathogenesis of the disease reported in the literature as extramammary Paget's disease.

Three cases are presented which offer, respectively, clinical, histologic and clinical and histologic features of Paget's disease.

Criteria are discussed by which Paget's disease can be differentiated from similar diseases (Bowen's disease, erythroplasia and superficial epidermoid carcinoma).

46. Lang, M., cited by Beck.[16]

In accordance with the views of previous authors, Paget's disease of the nipple is defined as the expression of a more or less well balanced symbiosis of the epidermis and an epidermotropic strain of cancer cells of mammary origin.

It is proposed to designate the interesting and unique biologic phenomenon of symbiosis of epidermis and "Paget cell" as the "Paget phenomenon."

On the basis of this biologic conception it appears justifiable to include as instances of Paget's dermatosis all those cases in which the Paget phenomenon is present, Paget's disease of the nipple being only its most frequent and best known example.

Extramammary Paget's dermatosis is due to the intraepidermal spread (*a*) of carcinoma of the apocrine glands (and perhaps of other cutaneous glands), (*b*) of carcinoma of mucous membranes bordering on the skin and (*c*) possibly of melanoblastoma.

RHINOSCLEROMA

REPORT OF TWO CASES

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At the symposium on rhinoscleroma at the International Oto-Rhino-Laryngological Congress in Madrid, Spain, in 1932,[1] 2,631 cases were reported; 51 from the United States, 11 of native patients. J. W. Jervey, who examined our first patient, has been quoted by Jackson [2] as suggesting that a foyer of rhinoscleroma is present in South Carolina.

CASE 1.—D. H. J., a white married woman aged 41, from Greenville, N. C., had never been outside the United States except for a short trip to Canada. She had spent most of her life in the Piedmont section of South Carolina, but had lived in Washington, D. C., from 1916 to 1924, except for nine months during 1917 to 1918 when she resided in Newport News, Va. She was first seen in April 1924 (by C. A. S.) for a condition of the nose which had been present for four years. In June 1923 Dr. Oscar Hunter, of Washington, D. C., cultured the Frisch bacillus in material from the nose and observed Mikulicz cells in microscopic sections.

Examination showed on each side of the septum a cyanotic whitish firm nodular lesion covered by a slight scale. The patient received interstitial applications of a total of 470 milligram hours of radium in 10 mg. steel needles (equivalent to filtration with about 1 mm. of aluminum) from April to September 1924. She was not seen again by us, but Dr. J. W. Jervey, of Greenville, S. C., who examined her in November 1937, could not find any signs of rhinoscleroma. In 1928 he had explored the sphenoid and ethmoid sinuses, and at that time, in performing a submucous resection of the septum, he found the overlying soft structures to be atrophic and firmly attached to the bone.

CASE 2.—A. R., a white married woman aged 55, was first seen in May 1937, complaining of an enlargement of the nose of three years' duration. The patient was born in England but in recent years had returned to her native land only about every third summer. The entire end of the nose was enlarged and somewhat bulbous, but smooth, firm and of a dull violaceous color. Within the nose, attached to each side of the septum, there were nodules of approximately 1 cm. similar in appearance to that on the end of the nose. The surface showed a few dilated follicles. No scales, crusts or telangiectases were seen. The part of the nodule on the right side of the septum was removed for section. Many unsuccessful attempts were made to culture Frisch bacilli in material from the nose and from the tumor itself.

From the Department of Dermatology, George Washington Medical School.

1. Staikoff, S. M.: Le scleroma, Cong. internat. d'oto-rhino-laryng. Madrid, 1932, p. 352.

2. Jackson, C., in Rapports sur le sclérome, International Congress of Oto-Rhino-Laryngology, Sofia, S. M. Staikoff, 1932, p. 352.

Fig. 1 (case 2).—External involvement of the nose.

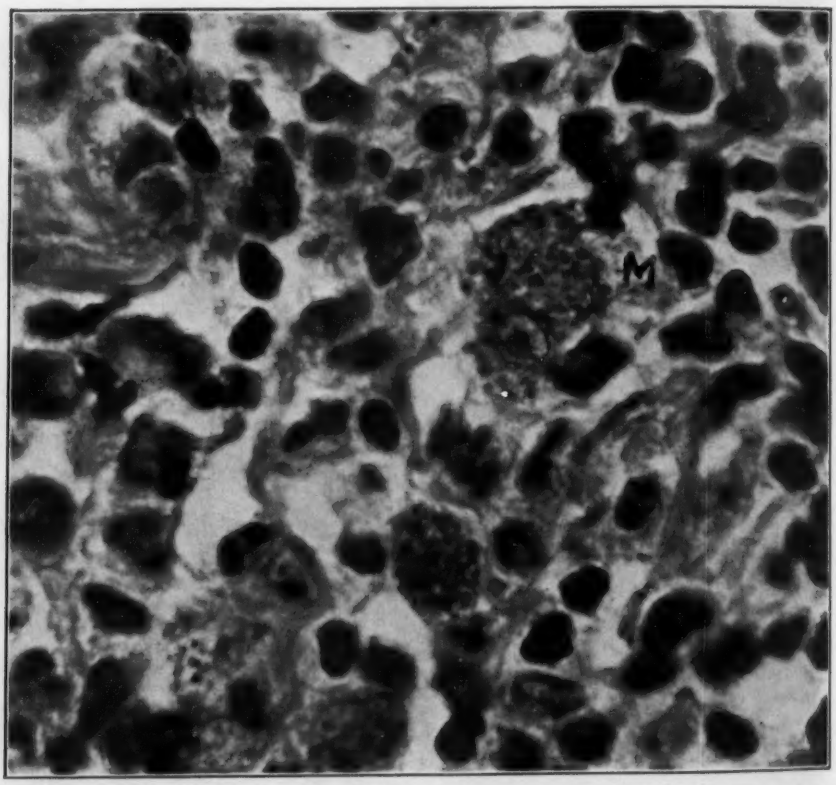

Fig. 2 (case 2).—Section showing large Mikulicz cells (*M*).

General physical examination showed no abnormality. Laboratory findings were essentially normal. Agglutination, complement fixation and cutaneous sensitization tests were not performed, because the necessary material was not available.

Histologic Examination.—Under low power the epidermis over the area of infiltration appeared atrophic and was covered with a thin layer of keratin. The infiltrate was dense in the upper layers of the cutis and was concentrated in foci, but there was a diffuse infiltrate that extended throughout the entire section. The blood vessels were increased, with many dilated capillaries and arterioles. Many of the latter had small lumens and thickened walls. Much brown pigment and fibrosis were present.

High power magnification showed the epidermis to be atrophic, with some intracellular edema. The areas of dense infiltrate were composed of small lymphocytes, many eosinophilic leukocytes, some neutrophilic polymorphonuclear leukocytes, plasma cells and chromatophores and a few large cells (about 20 microns in diameter), with a foamy or coarsely granular cytoplasm (Mikulicz cells). Many sections were examined before Russell bodies were found. Some areas contained many fibroblasts. The area with the less dense infiltrate contained mostly lymphocytes, polymorphonuclear leukocytes and fibroblasts. Perles' stain showed no iron. Bacterial stains showed that the large foam cells contained short rodlike bodies (Frisch bacilli?).

COMMENT

Two cases of rhinoscleroma are reported. The first patient, from the southeastern states, was cured with radium and has remained well for fourteen years. The second patient also was treated with radiation but has shown no appreciable results; however, it is important to mention that at the time the first patient left our care she too had not shown any definite signs of improvement.

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KARAYA GUM AS A CAUSE OF URTICARIA

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The first author to cite karaya gum as an allergen was Bullen.[1] Later Feinberg [2] and more recently Figley [3] added 9 cases. During the past two years this atopen has been responsible for urticaria in 5 of my patients. One patient had, in addition, an obstinate attack of respiratory allergy. The following report of one of the 5 cases is representative of the clinical features and investigative difficulties involved.

REPORT OF A CASE

G. K. L., a woman aged 31, came to the clinic in December 1937 because she had suffered for eighteen months from periodic episodes of pruritus, urticaria and angioneurotic edema. At the onset of each attack there was severe pruritus, which became so distressing that sedatives and mechanical restraints were of no avail. Within a short period generalized urticaria developed, accompanied by a few lesions usually classified as angioneurotic edema. It is interesting to note that during none of the attacks were the soles or the tongue involved. There was, however, frequent involvement of joints, though the articular edema never progressed to the point of limitation of motion.

As the urticarial phase of the cycle subsided, there appeared at the sites of the previously edematous areas brown hyperpigmentation which was so persistent that the skin failed to regain its normal color in the intervals between exacerbations. The appearance of the lesions in both the acute and the quiescent periods strongly suggested the fixed exanthem produced by the ingestion of certain drugs, especially phenolphthalein. The error of this conjecture was established by the fact that administration of phenolphthalein failed to reproduce any part of the clinical features of this patient's malady.

History.—Pneumonia occurred during infancy. All teeth had been removed. The patient had worn a lower plate for ten years and an upper plate for six years. I was unable to demonstrate sensitivity to external heat or cold.

There was no family history suggesting allergy except that a brother of the patient had "sick headaches." Urinalysis, gastric analysis and examination of the blood all gave normal results, and the Wassermann reaction of the blood was negative.

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1. Bullen, S. S.: J. Allergy **5**:484 (July) 1934.

2. Feinberg, S. M.: Karaya Gum Asthma, J. A. M. A. **105**:505 (Aug. 17) 1935.

3. Figley, K. D.: Toledo, Ohio, Allergy International Correspondence Club, 1938, p. 7; personal communication to the author.

The patient was an evangelist who had followed an active preaching program. However, after eleven years of such a vocation, I felt that psychogenic factors should be minimal. She volunteered the information that her only worry was financial.

There was no history of ingestion of any drug prior to the onset of the syndrome aforementioned. Numerous tentative dietary regimens had been followed, without benefit.

Exhaustive studies of the food and the environment and tests with pollen all gave negative results. Patch testing was done with plates; the results were negative.

Urticarial and pigmentary changes suggesting fixed exanthem due to phenolphthalein, secondary to Karaya gum.

The upper dental plate fitted improperly. Because of this the patient had used Wernet's dental powder for eighteen months. I tested with the active principle in this powder, karaya gum, or Indian gum, and obtained a strongly positive result by the scratch method. (Although karaya gum is difficult to prepare for intradermal testing, this can be done if a solution is heated for one hour on three successive days. The preparation may also be obtained from certain firms that make antigens for testing.)

Physical Examination.—The patient weighed 114 pounds (51.7 Kg.), was prematurely gray and had a blood pressure of 108 systolic and 72 diastolic. Her physical development was normal.

On the body, particularly on the hands, there were multiform edematous lesions with an erythematous base. Many had a bronzed cap. Several areas exhibited typical urticaria, but there were numerous macular islands showing only brown hyperpigmentation.

Progress.—After the use of the dental powder was discontinued all symptoms abated in a few days. The powder was then used as formerly, and immediately the original symptoms returned. It was then advised that the ill fitting plate be replaced. This was done, and at the time of writing, after ten months, the patient reports complete freedom from urticaria.

There are still a few islands of hyperpigmentation, but the skin elsewhere is normal. However, a unique complication is now present in that three finger nails have been lost.

SOME PROPERTIES OF KARAYA GUM [4]

Karaya gum [4] is commonly called Indian gum. Bassora gum is a collective term used to indicate a group of high-colored gums physically allied to tragacanth. True Indian gum is a fine white powder with an odor resembling that of dilute acetic acid and is soluble in water. This gum is derived from a tropical tree of the Sterculia family, which is indigenous to southern Asia and India. To this group also belong Bassora gum, Sterculia gum, and ghatti gum.

As has been pointed out by Figley,[3] the nitrogen content of karaya gum is only 0.1 per cent. In spite of this low nitrogen content, true sensitivity to this gum can be very severe.

SOURCES OF KARAYA GUM [5]

1. Saraka [6]
2. Kara jel
3. Karaba
4. Gum drops
5. Some ice creams
6. Ice cream liquid mix
7. Prepared ice cream powders
8. Certain brands of gelatin; [7] Junket
9. Many hand lotions
10. Hair-fixing solutions.
11. Tooth pastes
    (*a*) Listerine
    (*b*) Lactona

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4. Wood, C. H.; La Wall, C. H., and others: The Dispensatory of the United States of America, ed. 22, Philadelphia, J. B. Lippincott Company, 1937, p. 1400.

5. Figley's list supplemented by the author's personal investigation.

6. Products responsible for allergic conditions in my 5 cases of sensitivity to Karaya gum.

7. Knox gelatin contains no Karaya gum.

12. Denture adhesive powder
    (*a*) Doctor Wernet's powder [6]
    (*b*) Dent-a-Firm
    (*c*) Denture powder
    (*d*) Stix
13. Some candies with soft centers
14. Diabetic foods, including soy bean and almond wafers
15. Many emulsfied mineral oils and laxatives
16. Mucara (John Wyeth) [6]
17. Imbicoll (Upjohn) [6]
18. Bassoran (Merrell)
19. Fillers for lemon, custard and other factory-made pies
20. Karabim (Geo. A. Brown & Co.)
21. Commercially prepared ices and flavor emulsions; some salad dressings

SUMMARY

Five cases of hypersensitivity to karaya gum are added to the number already reported in the literature. One of these is reviewed in some detail because the clinical course in this instance closely simulated both urticaria and a hyperpigmented fixed exanthem usually seen after the administration of certain drugs.

Figley's list of environmental sources of karaya gum has been supplemented. Because of the multiplicity of these sources it is recommended that this gum be employed as test material in all cases of allergy in which the cause is obscure. The case also demonstrates that a good history is often more revealing in cases of allergy than is unlimited cutaneous testing.

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INADEQUACY OF THE LAUGHLEN AND THE IDE TEST IN THE DIAGNOSIS OF SYPHILIS

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PHILADELPHIA

Within the past three years two new tests, the Laughlen and the Ide, have been introduced for the serodiagnosis of syphilis. These tests are called "color tests" and differ from the usual flocculation test in that a dye is added which makes the clumped antigen in a positive reaction more visible. Shortly after the publication of Laughlen's report, prepared antigen was put on the market for use in laboratories and by private physicians. The Ide antigen can likewise be purchased. It is the purpose of this paper to present the results of a comparative study of these tests with the Kline, the Kahn and the Kolmer complement fixation test, in order to inform those performing these tests without controls of what they may expect in the way of specificity and sensitivity. No attempt has been made to improve on the procedures, and directions furnished by the distributors were followed.

Originally Laughlen [1] stated that his test could be used on raw or citrated serum. However, these statements were retracted,[2] and it was advised that serum be heated at 56 C. for ten minutes or at 63 C. for three minutes. It was also advocated that spinal fluid be treated with ammonium sulfate to concentrate the globulin. Full details as to the preparation of the Laughlen antigen appeared in his original publication; [1] essentially it consists of cholesterolized Kahn antigen to which has been added tincture of benzoin and scarlet red. The reagent is activated by addition of a specific amount (determined by previous titration) of 10 per cent solution of sodium chloride to 1 cc. of stock

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The antigen for these tests was supplied by C. H. Rein, of New York, and H. Beerman, of Philadelphia.

From the Department of Dermatology and Syphilology, School of Medicine, University of Pennsylvania; John H. Stokes, M.D., Director.

1. Laughlen, G. F.: Rapid Test for Syphilis, Canad. M. A. J. **33**:179 (Aug.) 1935.

2. Supplementary Note Regarding Laughlen Reagent, Lederle Laboratories, Inc., Pearl River, N. Y. (Note contained in directions sent with each bottle of antigen.)

solution. After standing for twenty-four hours at room temperature, the antigen is ready for use.

The Ide test is recommended for use on whole blood, serum or citrated blood, inactivation not being necessary. Directions for preparing the antigen were given in full in the original article of Ide and Ide.[3] The antigen is an alcoholic beef extract to which have been added cholesterol, benzoin, methyl rosaniline and azure II. Before use, 0.2 cc. of the antigen is diluted with 0.6 cc. of 2.5 per cent solution of sodium chloride.

The two tests are conducted similarly, in that 0.03 cc. of serum is allowed to flow on a clean slide. A drop (0.03 cc.) of antigen is added, and the slide is rotated until the serum and antigen are well mixed. In the Laughlen test inactivated serum is used and the result is read macroscopically. In the Ide test raw serum is used, and the microscope is needed for reading the reaction. We found the Laughlen reaction comparatively easy to read, but some difficulty was experienced in reading the Ide reaction.

Robinson and Stroud [4] and Price [5] reported favorably on the Laughlen procedure. Rein and Hazay [6] found the test less specific and less sensitive than the Kline test and stated that it, as well as others like it, is not a safe procedure in the hands of the inexperienced operator. In the discussion of their paper Kahn further emphasized the necessity for an expert to conduct tests for syphilis. Usher's [7] experience with the Laughlen test was that it was less specific, and when the sensitivity of the reagent was reduced sufficiently to eliminate false positive reactions it failed in a significant number of instances to detect reagin in serum which gave a positive reaction to the Eagle flocculation test. This study prompted an editorial [8] warning against use of the Laughlen test by an untrained person. The majority of reports [9]

3. Ide, S., and Ide, T.: Ide Test—A New Color Test for Syphilis, J. Lab. & Clin. Med. **21**:1190 (Aug.) 1936; Klin. Wchnschr. **15**:973 (July 4) 1936.

4. Robinson, F. H., and Stroud, G. M.: Laughlen's Test for the Serodiagnosis of Syphilis, J. A. M. A. **108**:1170 (April 3) 1937.

5. Price, A. S.: The Laughlen Agglutination Test for the Serological Diagnosis of Syphilis, M. Times, New York **65**:398 (Aug.) 1937.

6. Rein, C. R., and Hazay, C.: The Laughlen Test for Syphilis, J. Invest. Dermat. **1**:283 (Aug.) 1938.

7. Usher, G. S.: An Appraisal of the Laughlen Serologic Test for Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **22**:452 (July) 1938.

8. The Laughlen Test for Syphilis, editorial, Am. J. Syph., Gonor. & Ven. Dis. **22**:517 (July) 1937.

9. (*a*) Ide, S., and Ide, T.: Un nouveau test pour le diagnostic de la syphilis, Ann. d. mal. vén. **32**:321 (May) 1937. (*b*) Honda, T.: Beiträge zur Ide-Reaktion, J. Kumamoto M. Soc. **13**:774 (April 20) 1937. (*c*) Hanazono, M.: Ueber die Idesche Syphilisreaktion und Dahrsche Reaktion, J. Chosen M. A. (Abstr. Sect.) **26**:37 (Aug. 20) 1936. (*d*) Quisumbing, M.: Ide's New Coloring Test for Syphilis, J. Phillipine Islands M. A. **16**:609 (Oct.) 1936.

on the Ide test are abstracts from or translations of the original publications,[8] except those of Oliveira de Almeida [10] and Bartolozzi,[11] who reported favorably on 106 and 319 specimens of serum, respectively. Rein and Hazay [12] obtained agreement with the Kline test of syphilitic serum (inactivated) in 97.11 per cent and with three complement fixation procedures in an average of 91.59 per cent of cases. He likewise found the Ide test less specific.

The specimens of blood used in this study were obtained from patients in the dermatologic and syphilologic clinic of the University of Pennsylvania. The specimens were divided into syphilitic and nonsyphilitic, the nonsyphilitic blood being from patients with various cutaneous diseases, those who had come for syphilologic investigation which proved to be negative and a few nonsyphilitic neurologic patients. The syphilitic group was divided into specimens from patients who had received treatment and from those with untreated disease, classified as early, including primary, secondary and relapsing secondary syphilis; latent, late cutaneous, bony and visceral syphilis, and syphilis of the central nervous system. All patients were submitted to complete physical examination.

The tests were checked by the Kline slide precipitation test, the Kahn standard test and a two tube Kolmer complement fixation test (0.1 and 0.05 cc. of serum being used). There was remarkable absolute and relative agreement of these three tests, 100 per cent in the series studied. Their agreement was further checked in a review of 5,279 tests done in one year. Of the tests performed, disagreement was noted as follows:

No.	Kline	Kolmer	Kahn
203	Negative–1 plus	00	000
24	Negative–1 plus	00	012
1	Negative–1 plus	00	122
4	Negative–1 plus	11	000
1	Negative–1 plus	44	122
1	Negative	11	012

This gives a disagreement of about 4 per cent, and when the Kline reaction of the first group of 203, negative–1 plus, is rated as negative, the percentage of disagreement drops to less than 0.6. With this degree of conformity it was not necessary to compare separately the Kline, the Kahn and the Kolmer with the Laughlen and the Ide test.

10. Oliveira de Almeida, J.: O sôro-diagnostico da syphilis pela reacção de Ide, Brasil-med. **51**:278 (Feb. 13) 1937.

11. Bartolozzi, M.: La nuova reazione colorata di Ide per la diagnosi di sifilide, Rinasc. med. **14**:299 (May 15) 1937.

12. Rein, C. R., and Hazay, C. E.: Ide Test for Syphilis: A Comparative Study with Kline Heated Serum Tests and Complement Fixation Methods, with a Clinical Evaluation in More Than One Thousand Patients, J. Lab. & Clin. Med. **23**:954 (June) 1938.

RESULTS

In the nonsyphilitic group, the Laughlen and control tests agreed for 307 of 314 specimens, or 97.78 per cent. There were 4 false positive reactions to the Laughlen test (1.27 per cent) and 3 to the control tests (0.95 per cent). The Ide test was performed on 257 specimens, with an agreement on 246 specimens, or 95.72 per cent. There were 8 false positive Ide reactions in this group (3.11 per cent). This indicates that the Laughlen and Ide tests are less specific than the standard test used.

In the cases of treated syphilis 507 specimens were used for the Laughlen and 404 specimens for the Ide test. There was agreement on 387 specimens, or 76.33 per cent, with the Laughlen test and on only 57.43 per cent (232) with the Ide test. The Kahn, the Kline

Examinations of Spinal Fluid (Not Inactivated or Concentrated)

Case	Cell Count	Globulin Reaction	Colloidal Curve Mastic	Wassermann Test	Laughlen Test	Ide Test
1	10	4+	4555552100	4444	Negative	Positive
2	18	4+	5555554310	4444	Negative	Positive
3	18	4+	5555421000	4444	Negative	Positive
4	86	4+	3555421100	4444	Negative	Positive
5	40	4+	5555421000	4444	Negative	Positive
6	8	4+	5555421000	4444	Negative	Positive
7	6	3+	4554321100	2344	Negative	Positive
8	6	4+	5543110000	2344	Negative	Positive
9	6	2+	2221100000	0122	Negative	Negative
10	5	2+	2221110000	0011	Negative	Negative
11	4	1+	2221100000	0011	Negative	Negative
12	4	Negative	1111100000	0000	Negative	Positive
13	4	Negative	1110000000	0000	Negative	Positive
14 to 40	0 to 4	Negative	Negative	0000	Negative	Negative

and the Kolmer test remained positive in 108 cases (21.3 per cent), while the Laughlen test was negative and in 163 cases (40.34 per cent) while the Ide was negative. The Laughlen and the Ide test were positive while the control tests were negative in 12 and 9 cases, respectively, or 2.37 and 2.23 per cent. Thus it is evident that the Laughlen and the Ide test become negative during treatment sooner than the standard tests.

The Laughlen test gave an agreement of 89.48 per cent (51 cases) in the group of 57 cases of untreated early syphilis and failed to detect the disease in 6 cases, or 10.52 per cent, in which the control tests gave positive results. The Ide test was less satisfactory, detecting the disease in only 18 cases out of 43, or 41.83 per cent. Neither the Laughlen nor the Ide test was positive in the cases in which the control tests were negative.

Of the 147 specimens from patients with untreated late syphilis the Laughlen test agreed on 95, or 64.63 per cent. There were 48 cases (32.65 per cent) in which the Laughlen reaction was negative and

the Kahn, the Kline and the Kolmer positive. In only 4 cases was the Laughlen reaction positive and the control negative. The Ide test, as in the other group, was inferior to the control tests, in that agreement was present in only 40 cases out of 118, or 33.9 per cent. There were 75 cases (63.56 per cent) in which the Ide test was negative and the control test positive. The opposite was true in only 3 cases.

The table gives the results obtained by examination of the spinal fluid in 40 cases. The fluid was not concentrated or inactivated. The first 13 specimens were from patients with neurosyphilis, the remainder having no evidence of neurosyphilis either by previous examination of the spinal fluid or by neurologic examination.

Of the total of 1,025 Laughlen tests performed, there was agreement in about 81.95 per cent, and on 67.93 per cent of the 711 specimens of syphilitic serum. Only about half (51.32 per cent) of the Ide tests agreed with the standard tests performed on 565 specimens of syphilitic serum. Of the total of 822 Ide tests, there was agreement in 61.11 per cent. We are at a loss to explain these poor results. All the antigens were made by reliable commercial houses [13] and came to us in the original packages. The technic was carefully checked, and all tests were read by both of us.

SUMMARY

A comparative study of the Laughlen and the Ide test with the Kline, Kahn and Kolmer tests is presented.

Tests were performed according to directions supplied by the distributors of the antigens.

CONCLUSIONS

1. The Laughlen and the Ide test are less specific than the three standard tests used.

2. The Laughlen and the Ide test are inadequate for the serodiagnosis of syphilis.

3. The Ide test is satisfactory for the examination of spinal fluid, but the Laughlen test grossly fails when the spinal fluid is not concentrated.

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13. The Laughlen antigen was made by the Lederle Laboratories, Inc., Pearl River, N. Y., and the Ide antigen (Idechon), by the Owl Manufacturing Co., Tokyo, Japan.

PEMPHIGUS CONTROLLED BY VITAMIN D

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In 1932 Ludy [1] reported 6 successive cases of pemphigus in which the condition was apparently cured by large doses of viosterol and ultraviolet ray therapy. His results led to the trial of concentrated viosterol in this case.

REPORT OF A CASE

Dr. E. L. A., a white man aged 65, married, a college president, was first seen June 11, 1936. The chief complaint was a pruritic, painful erythematobullous eruption completely covering the feet, the legs, the lower parts of the thighs, the hands and the forearms. It consisted of widely separated, discrete lesions on the upper parts of the thighs, the hips, the back, the arms, the shoulders, the upper part of the chest, and the neck. The face, scalp, abdomen and mucous membranes were not involved. The prevailing lesions were bullae 1 to 3 cm. in diameter, situated on erythematous bases. A few bullae appeared without the erythematous areola.

A diagnosis of pemphigus vulgaris was made despite the absence of Nikolsky's sign. The temperature was 99.2 F. and the pulse rate 76.

The patient stated that the eruption had occurred five weeks previously on the forearms, the legs and the ankles and that a competent dermatologist had made the diagnosis of trichophytid one week after the onset but had soon changed it to erythema multiforme bullosum.

The past history was unimportant. The patient had been a hard worker at the head of a college for twenty-five years, had kept irregular hours and had eaten a poorly balanced diet.

He was of medium height and well nourished. The muscular tone was good. General examination gave negative results.

The Wassermann reaction of the blood was negative. The hemoglobin content was 84 per cent (Sahli). There were 9,600 white blood corpuscles and 3,740,000 red corpuscles per cubic millimeter. The differential count showed: polymorphonuclears, 41.5 per cent; small lymphocytes, 22.5 per cent; large lymphocytes, 5.0 per cent; eosinophils, 30.5 per cent, and basophils, 0.5 per cent. The value for calcium was 8.6 mg. per hundred cubic centimeters. The urine was normal.

Treatment was started with neoarsphenamine in doses of 0.3 Gm., 0.45 Gm., 0.6 Gm. and 0.6 Gm. at intervals of three days for the first two doses and five days for the last two. This was supplemented by 3 cc. of viosterol three times a day. In the meantime the eruption spread to all parts of the body and became more bullous. One or two lesions developed in the mouth and Nikolsky's sign could be easily demonstrated.

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1. Ludy, J. B., and DeValin, C. M.: Viosterol in the Treatment of Pemphigus, Urol. & Cutan. Rev. **36**:817 (Dec.) 1932.

It was decided to change to the Davis [2] plan of treatment with iron cacodylate and coagulen. This was carried out for two weeks, without improvement. The maximum temperature was 102 F., and the greatest pulse rate was 120. The patient had lost considerable weight, was losing his appetite and was sleeping poorly. Codeine and occasionally morphine were required for relief. Two blood transfusions of 300 cc. each were given three days apart, without apparent benefit. Dr. Joseph Grindon [3] was consulted; he concurred in the diagnosis and recommended coagulen and five doses of tryparsamide to be given every five days in the following amounts: 1 Gm., 1.5 Gm., 2 Gm., 2 Gm. and 2 Gm. When this procedure failed, Dr. Grindon advised the substitution of moccasin snake venom, which was given for three and a half weeks according to the Peck [4] plan. The lack of benefit and the appearance of local reactions caused this treatment to be suspended on October 11, at which time the temperature ranged from 100 to 104. The pulse rate fluctuated between 100 and 120, and the pulse was very weak. The patient was stuporous and at times semidelirious.

The failure of well recognized remedies used for five months and the report of Ludy's results with viosterol and ultraviolet therapy led to the trial of concentrated viosterol in capsules each containing 50,000 U. S. P. (international) units of vitamin D.[5] The patient was given 3 capsules a day and showed improvement within a week. The dose was gradually increased to 400,000 units daily, and in four weeks the improvement was remarkable, but the patient had nausea and epigastric distress and became apathetic. The dose was reduced to 200,000 units per day, and the untoward symptoms soon disappeared. In the meantime the bullae cleared up, but Nikolsky's sign could still be readily elicited. The daily dose was reduced to 100,000 units, and the treatment was discontinued in about one week. The patient gained strength and was soon able to walk. After a week severe pruritus and a few bullae began to recur. A daily dose of 300,000 units was again prescribed, and in a few days the skin was clear. The patient was dismissed from the hospital November 28. He returned home, took 300,000 units of the vitamin daily for approximately three weeks and again had nausea, epigastric distress and mental apathy. On one occasion he fainted and remained unconscious a few minutes. Administration of the vitamin was again suspended, whereupon the symptoms were controlled, but in about two weeks a few bullae reappeared. He was given 200,000 units of vitamin D daily, and in a few days the skin was clear. He went to Florida for the winter, and the daily administration of 200,000 units of the vitamin for a month resulted in slight nausea and loss of appetite. The dose was reduced to 100,000 units a day and was kept at that level for about a year. During this period the patient regained his normal weight and strength, and the blood picture practically returned to normal. The treatment was terminated in the fall of 1937 by administration of 50,000 units daily for a short time.

This case was observed from June 11, 1936 to Oct. 1, 1938. At the time of writing the patient's appetite is good, he sleeps well, and he is able to work with full concentration for six or eight hours a day.

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2. Davis, R. H., and Davis, W. D.: A Contribution to the Treatment of Pemphigus, Arch. Dermat. & Syph. **8**:627 (Nov.) 1923.

3. Grindon, J.: Tryparsamide in Acute Pemphigus, Arch. Dermat. & Syph. **21**:25 (Jan.) 1930.

4. Peck, S. M.: Pemphigus Treated with Moccasin Venom, Arch. Dermat. & Syph. **33**:150 (Jan.) 1936.

5. The vitamin D used in this case was supplied by the Wm. S. Merrell Co., of Cincinnati.

COMMENT

The patient had the well recognized symptoms and cutaneous manifestations of pemphigus vulgaris, which had progressed to a state of grave disease. The Davis, the Grindon and the Peck plan of treatment were tried for periods of two to four weeks each, the patient progressively losing ground.

With the institution of highly concentrated vitamin D therapy, the patient began to improve at once, and he was ultimately relieved of symptoms.

Vitamin D was given in capsules containing 50,000 U. S. P. units each.

Administration of the vitamin in doses of 300,000 to 400,000 units a day for three or four weeks controlled the cutaneous lesions but caused disagreeable symptoms (nausea, slight epigastric distress, mental apathy and general weakness). When the dose was reduced to 50,000 or 100,000 units the patient remained both free of cutaneous lesions and without symptoms of hypervitaminosis.

At the time of writing, eleven months after discontinuation of the therapy, there has been no recurrence of the disease and no ill effect from the treatment.

SUMMARY

A case of pemphigus is reported. The condition was apparently controlled by tremendous doses of vitamin D in high concentration.

When a certain dose was attained, untoward symptoms occurred.

This experience tends to show (*a*) the amount of the drug which may be necessary to control pemphigus, and (*b*) the toxic dose for an adult.

SENSITIVENESS OF SKIN TO ROENTGEN RAYS FOLLOWING INGESTION OF ARSENIC

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Several years ago, at a meeting of the Minnesota Dermatological Society, the therapy of superficial cutaneous epithelioma was discussed. One of the members expressed the opinion that epithelioma following the ingestion of arsenic and containing abnormally large amounts of arsenic was extremely resistant to radiotherapy. Somewhat later one of us encountered extraordinarily severe cutaneous reactions following roentgen therapy to several superficial epitheliomas in a patient with psoriasis who had ingested solution of potassium arsenite over a period of years and who had, in addition to multiple malignant growths, arsenical keratoses on the palms and soles. These events stimulated interest in the question of whether arsenic in any way influenced the radiosensitiveness of the skin.

Judging from the extremely few references in the literature to the relation of arsenic to radiosensitiveness, one might infer that if arsenic had any material effect on the reactivity of the skin to irradiation the problem would have been studied in detail long ago. On the other hand, some effect has at least been suspected. Blumenthal [1] expressed the belief that arsenic (given in the form of sodium arsanilate) enhanced the effects of irradiation in cases of malignant tumor. Voltz [2] stated that the irritating effect of arsenic in tissues might increase the effect of irradiation. Epstein [3] stated that he had been warned to be cautious in the administration of radiation to patients who were ingesting arsenic. Naegeli [4] stated that patients who were taking arsenic during roentgen therapy were more prone to pigmentation than others. He stated that

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From the Division of Dermatology, University of Minnesota, H. E. Michelson, M.D., Director; and the Dermatology Service, Minneapolis General Hospital, S. E. Sweitzer, M.D., Chief.

1. Blumenthal, F.: Ueber das therapeutische Problem bei den bösartigen Geschwülsten, Deutsche med. Wchnschr. **47**:1151, 1921.

2. Voltz, F.: Sensibilität und Sensibilisierung in der Strahlentherapie, Fortschr. a. d. Geb. d. Röntgenstrahlen **29**:61, 1922.

3. Epstein, S.: Personal communication to the authors.

4. Naegeli: Röntgenschädigungen, Schweiz. med. Wchnschr. **58**:212, 1928.

from this standpoint arsenic might be regarded as a sensitizing agent and cautioned against irradiating the faces of patients who were receiving arsenical therapy.

For years arsenic headed the list of remedies used for the internal treatment of various dermatoses, because of its effect on the skin and particularly the epidermis. This holds true for both the inorganic and organic forms. The propensity of arsenic to cause erythematous or exfoliative toxic eruptions, to increase the production of pigment in epidermal cells, to cause epidermal proliferation to the point of keratosis and even malignant growth and to cause congestion and irritation of the cutaneous vascular system make one at least suspect that the drug influences radiosensitiveness.

EXPERIMENTAL STUDIES WITH ROENTGEN RAYS AND ARSENIC

The patients in this study were divided into the following three groups:

1. Thirty-four who were exposed to roentgen rays before the ingestion of inorganic arsenic.

2. Thirty-three who were exposed after the ingestion of inorganic arsenic.

3. Thirty-four who were exposed during courses of organic arsenical (neoarsphenamine) antisyphilitic therapy.

Twenty-three of the aforementioned nonsyphilitic patients were tested both before and after the ingestion of the arsenic. Eleven other patients were tested before the ingestion of arsenic and failed to return for further study. Ten additional patients who had not had the preliminary study were given arsenic and tested. The medication in all cases was the "Asiatic" (arsenic) pill.[5] A total of 100 such pills were given at the rate of 3 daily, 1 before each meal. The patients were retested just after the supply of tablets was finished.

All the syphilitic patients were receiving neoarsphenamine intravenously before and after the irradiation and during the roentgen reaction.

The exposures to roentgen rays were made on the anterior surfaces of the thighs through round portals 2.5 cm. in diameter. Each portal was spaced 5 cm. from the next one. As a routine, four doses, of 75, 150, 225 and 300 r, were delivered by a General Electric machine (mechanically rectified), which was calibrated at the start of the experiment. A total of 18 syphilitic and 25 nonsyphilitic patients were given an additional dose of 375 r. The following factors were used: 100 kilovolts, 8 milliamperes, 12 inches (30.5 cm.) and no filtration.

5. According to the manufacturer's catalogue each pill contains 1/6 grain (0.007 Gm.) of arsenic trioxide and 1 grain (0.06 Gm.) of black pepper and the pills are "to be used cautiously on account of large doses of arsenic trioxide."

After the tests an attempt was made to observe the reactions two or three times weekly. In many instances, however, the patient failed to return more frequently than weekly. These cases were considered in the study, since it was possible to obtain sufficient data at these intervals to compare the length and degree of the roentgen reaction. The records of patients who were irregular were not considered.

In all cases the patient was followed until the erythema (when present) had faded or had been replaced by pigment. Most of the patients who were tested in the fall of 1937 still showed sharply demarcated areas of pigmentation six months later. The readings were made by the same observer in all cases. The degree of erythema fol-

TABLE 1.—*Total Number of Patients in Whom Mild Erythema Followed Any Dose from 75 to 300 r*

Group	Total Number of Patients	Number with Erythema, Percentage	Number Without Reaction, Percentage
1	34	56.0	44.0
2	33	75.8	24.2
3	34	29.3	70.7

TABLE 2.—*Total Number of Patients in Whom Mild or Moderate Pigmentation Followed Any Dose from 75 to 300 r.*

Group	Number of Patients	Number with Pigment, Percentage	Number Without Pigment
1	34	91	9
2	33	91	9
3	34	86	14

lowing doses of 300 and 375 r was slight. No vesiculation or follicular reaction was noted. Cutaneous erythema to these doses was difficult to read, but it was felt that the errors in interpretation were minimized by the fact that the same observer recorded all the reactions. In 2 cases a dose of 600 r on the back produced vesiculation. An attempt was made in borderline erythema to differentiate the reaction from pigmentation by diascopic pressure.

For brevity the results of the experiments are given in tabulated form. The figures in the tables represent approximate percentages.

SPECIAL CASES

CASE 1.—G. M., a brunet man aged 62, took solution of potassium arsenite for four months in 1927. Neuritis and generalized pigmentation developed and the medication was discontinued. In September 1937 his skin was tested with

roentgen rays in doses up to 600 r, and no erythema appeared. Pigmentation of moderate degree was noted with all doses above 150 r.

CASE 2.—M. D., a brunet woman aged 42, had an exfoliative dermatitis and generalized pigmentation in October 1937, after the ingestion of solution of potassium arsenite. No erythema followed doses up to 300 r, although there was moderate pigmentation after 75, 150, 225 and 300 r.

CASE 3.—G. C., a brunet woman aged 64, took "arsenic pills" for an unknown length of time about twenty years ago. In September 1937 she presented multiple superficial epitheliomas, keratoses of the palms and soles and multiple psoriatic lesions. No erythema followed roentgen rays in doses as high as 300 r, but there was moderate pigmentation after all doses above 50 r.

CASE 4.—N. H., a red-haired woman aged 37, had a severe exfoliative crustaceous dermatitis due to neoarsphenamine in 1932. A similar exfoliation followed ingestion of acetylsalicylic acid in August 1937. In December 1937 she was tested with 75, 150, 225, 300, 375 and 450 r, but no erythema developed. Mild traces of pigmentation were noted after doses of 300, 375 and 450 r.

COMMENT

The results of our experiments with 78 patients coincided with those of Miescher [6] and MacKee and Eller [7] concerning the variations of cutaneous tolerance to roentgen rays. About one sixth of our patients reacted with a faint erythema to a dose of 225 r, approximately one half to 300 r and two thirds to 375 r. We obtained no erythema following 75 or 150 r in patients who had not ingested arsenic, whereas MacKee and Eller noted 4 to 5 per cent and 12 to 15 per cent, respectively, following the two doses. Reactions to 600 r showed considerable variation (mild pigmentation with no erythema up to actual vesiculation) in the few instances in which such a dose was given. The factors in the delivery of the roentgen rays were identical in all cases. The same machine and the same operator were used throughout the entire experiment.

We noted no material differences in the sensitiveness of blonds and brunets. Our figures, like those of Miescher, suggested that dark-skinned persons reacted more readily than blonds, at least to small doses. In 52 per cent of brunets, as compared to 40 per cent of blonds, erythema followed doses up to 300 r.

We did not compile statistics relative to age, since most of our patients were in the same general age group. There were no essential differences in the reactions of men and women.

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6. Miescher, G.: Das Röntgenerythem, Strahlentherapie **16**:333, 1923; Das Röntgenbiologie der gesunden und kranken Haut, ibid. **27**:257, 1927.

7. MacKee, G. M., and Eller, J. J.: Variations of Cutaneous Tolerance for Roentgen Rays, J. A. M. A. **87**:1533 (Nov. 6) 1926.

There were no notable differences in the reactivity of dry and oily skins, from the standpoint either of erythema or of pigmentation.

None of our patients were seriously ill, and no studies of blood were done; hence, the effect of general health or of anemia could not be considered.

In our group were several patients with cutaneous or other allergic manifestations, such as contact eczema, atopic dermatitis, hay fever, asthma, urticaria and dermatitis medicamentosa (other than arsenical). None of these patients showed reactions which could be considered abnormal from the standpoint either of erythema or of pigmentation when the tests were performed on areas of apparently normal skin. In 1 patient with chronic lichenified atopic dermatitis the tests were performed on areas of involvement. The amount of pigment was appreciably above the average, although no erythema developed after doses up to 300 r.

As Miescher brought out, the computation of average data is necessary to the drawing of any worth-while conclusions concerning various factors relating to the roentgen reaction. The long time required for the adequate study of such reactions renders the computation difficult, since it is only with great effort that the patients can be persuaded to return for sufficient observation. This was especially true in the experiment we performed, in which two sets of tests were done, one before and one after a month's ingestion of arsenic. To follow a single patient adequately required from four to six months.

Of the 34 patients (blonds and brunets) who were tested before the ingestion of Asiatic (arsenic) pills, 56 per cent reacted to doses of either 225 or 300 r. After the course of arsenic was completed, approximately 75 per cent had erythema after similar doses. Two patients who did not react to 300 r before medication had mild but definite erythema following 150 r after taking arsenic. On the other hand, some patients who had erythema following 300 r before the arsenic was taken had no erythema following the same dose after the medication was taken. Changes in the cutaneous reaction to the same dose of roentgen rays at different times are common; hence, such isolated observations are of little value. It will be noted from the report of special cases that none of the 4 patients who had received arsenic to the point of intolerance showed signs of increased radiosensitiveness. In cases 1 and 4 no erythema developed to 600 and to 450 r, respectively, showing that sensitiveness to roentgen rays, in these cases at least, was not an accompaniment of arsenical intolerance.

Of 34 patients taking organic arsenic (neoarsphenamine), in only 29 per cent did erythema develop after 300 r, as compared to 56 per cent for nonsyphilitic patients who had taken no arsenic. Although these figures permit no far reaching deductions, it is interesting to note

that the percentage was approximately as much below that of "normal" subjects as the percentage for patients who have taken inorganic arsenic (75) was above "normal."

As far as could be ascertained from our observations, arsenic had no influence on pigmentation produced by roentgen rays. In 91 per cent of patients pigmentation followed doses up to 300 r both before and after the ingestion of Asiatic (arsenic) pills. Two noteworthy features were: (1) that pigmentation developed in 78.5 per cent of blonds after doses of 75 r, as compared to 50 per cent for brunets (before arsenic) and (2) that in over half of all the patients pigmentation followed such low doses.

SUMMARY AND CONCLUSIONS

The following statements are made with the realization that the number of patients studied does not permit far reaching deductions. They are merely the records of our results:

1. No unusually strong reactions were encountered in any of the 78 patients after routine doses of 75, 150, 225 and 300 and, in 43 instances, 375 r.

2. One sixth of the patients had erythema following 225 r, one half following 300 r and two thirds after 375 r.

3. No important differentiation in radiotolerance could be made on the basis of sex, complexion or dryness or oiliness of the skin. In our group, erythema developed in 40 per cent of blonds and 52 per cent of brunets after 300 r.

4. Patients with various allergic diseases, such as asthma, hay fever, urticaria, dermatitis medicamentosa, atopic dermatitis and contact and nondescript eczema, showed no important variations from the normal reactivity.

5. In 50 to 80 per cent of patients mild pigmentation followed 75 r. After doses up to 300 r approximately 90 per cent of all the patients studied showed moderate pigmentation. In this series blonds showed a greater tendency to pigmentation than brunets. Arsenic had no apparent influence on the pigmentation in these cases.

6. The percentage of cases of mild erythema following doses of from 75 to 300 r increased from 56 to 75 after the administration of inorganic arsenic. In contrast, erythema developed in only 29 per cent of the patients receiving neoarsphenamine after doses of roentgen rays up to 300 r.

7. One patient who had arsenical pigmentation and neuritis, 1 with arsenical keratoses, 1 with an exfoliative dermatitis following the use of solution of potassium arsenite and 1 with a similar dermatitis following

the use of neoarsphenamine showed no increase in sensitiveness to roentgen rays.

8. It is believed that the changes of the reactions before and after the ingestion of the Asiatic (arsenic) pills and the low percentage of erythema in the patients receiving organic arsenic are best explained on the basis of ordinary variations at different times in the cutaneous tolerance to roentgen rays rather than on the basis of effects of the medication.

ABSTRACT OF DISCUSSION

DR. W. H. GUY, Pittsburgh: To those interested in the biologic effect of roentgen rays on the skin, this paper assumes the importance of a monograph. Its importance is enhanced by the fact that its introductory portion comprises a review of the world's literature on the subject and on related subjects.

The incidence and type of reaction from different types and amounts of radiation in patients of different complexion, age and sex are considered, and conclusions definitely pointed out. The necessary shortness of Dr. Laymon's presentation did not permit a detailed presentation of the pertinent literature.

One phase of the subject requires more than passing note: the question of individual susceptibility, a thing which all dermatologists have suspected for many years but which is difficult to prove. In a series of experiments on this subject some years ago I attempted, by placing the forearm of a suspected person beside that of another person and exposing both through a definite-sized window of radiopaque substance, to show variations in the susceptibility of the skin of different persons to varying doses. I was able in 1 or 2 instances to show that such a variation does occasionally occur. On working with 1 subject I observed a high degree of susceptibility, but I myself was more susceptible to the effect of irradiation, so far as the primary reaction was concerned, than the patient was.

On the other hand, in the late results, when one got up to the development of erythema, with a dose, say, of 300 r or more, pigmentation, ectasia and atrophy would always develop in my patient but not in me. Certainly an enormous amount of work must be done yet before the subject is completely clarified.

If there is one criticism to be made of the paper presented, it is in the way of a compliment: that the conclusions are ultraconservative.

I would call attention to the fact that reactions occurred in 29 per cent of cases after administration of organic arsenical preparations and in 75 per cent after the use of inorganic arsenical products.

The authors have been extraordinarily conservative in the interpretation of these results.

The difference demonstrated by Osborne and associates (Osborne, E. D.; Putnam, E. D., and Hitchcock, B. S.: The Effect of Arsenic on Rabbits, ARCH. DERMAT. & SYPH. **25**:419 [March] 1932) after the administration of organic and of inorganic arsenic, with reference both to location in the tissue and to the type of reaction of the tissue, should be borne in mind. The physicists say that the amount of reaction obtained in the tissues is in keeping with the amount of secondary irradiation produced, and that the amount of secondary irradiation

depends on the atomic weight of the tissue or substance irradiated. Perhaps herein lies an explanation for the increased reaction of the tissue in cases in which the inorganic type of arsenic is given.

It seems to me there is sufficient indication of such a possibility to warrant repetition of the experiments herewith reported.

Dr. Donald M. Pillsbury, Philadelphia: I think Dr. Laymon has discussed a most important subject: The individual variation in patients' susceptibility to roentgen rays and the factors influencing it.

Was the source of radiation the same throughout? It has been brought home rather forcibly to me in recent months, since I put in shock-proof therapeutic machines, that this uniformity is of great importance. In Dr. Laymon's experiments were roentgen rays of the same wavelength and of the same general quality used throughout?

It is known that with roentgen radiation in which there is a large proportion of long waves the effect is in general on a more superficial portion of the skin and that while unfiltered radiation is mentioned actually all this radiation is filtered, and the variation is rather great.

Because of the interest in shock-proof therapeutic apparatus at present, I investigated the matter fairly carefully before I put in a particular type of unit, and the general impression is now and was stronger previously that in tubes in which oil was used as the shock-proofing material the inherent filtration of the tube was high. However, the manufacturers, by cutting down the thickness of the port, have produced a tube which will emit soft radiation, and I found that in a particular tube which I used, the half value layer was 0.4 mm. Al equivalent whereas my old type tube was 0.8 mm. I found that this difference was quickly reflected in the results obtained; that in the performance of preliminary cutaneous tests, always employed before a patient is to receive prolonged open field irradiation, I obtained a higher percentage of pigmentary reactions with unfiltered radiation, and that occasionally pigmentation appeared after application of as little as 40 r to the face.

I think that consideration of the source as well as of things which produce variations in individual susceptibility is important.

Dr. Carl W. Laymon, Minneapolis: Dr. Guy suggested that the differences in cutaneous radiosensitivity before and after the ingestion of arsenic were great enough to be of significance. We had difficulty in interpreting the results but hesitated to conclude definitely that the inorganic arsenic raised the sensitivity of the skin to roentgen rays. There were some other points which, on account of lack of time, I could not bring out in reading the paper. For example, we had a small group of patients who were known to be intolerant to arsenic—patients with arsenical keratoses on the palms and soles, multiple carcinomas following the ingestion of arsenic, arsenical neuritis and arsenical dermatitis. All these patients seemed hyposensitive rather than hypersensitive to roentgen rays.

Dr. Pillsbury mentioned the source of radiation. In all cases the same man gave the test dose with the same machine, and in all instances the factors were the same. Low voltage (100 kilovolts) was used throughout the experiment. The machine was calibrated at the start and at the conclusion of the work. The same man read the erythema and the pigmentation in all cases, so as to minimize the possibility of error from that standpoint. It was difficult to interpret the milder degrees of erythema. An attempt was made to differentiate erythema from pigmentation by diascopic pressure.

One point might help persons doing similar experiments: In the beginning of the study the test doses were given at an 8 inch (20.3 cm.) distance with 8 milliamperes and 100 kilovolts. With doses even as low as 50 r, bright erythema developed on the following day. It was finally decided that the erythema appeared as a result of the heat from the tube, and when the distance was increased to 12 inches (30.5 cm.) and carbon paper was placed at the bottom of the tube, the early erythema was eliminated.

Clinical Notes

SITTING POSTURE FOR INTRAGLUTEAL INJECTIONS

THEODORE CORNBLEET, M.D., CHICAGO

Intramuscular injections for the treatment of syphilis and other diseases are made so frequently in everyday practice that anything which improves their technic should be welcomed. One of two positions, the standing and the recumbent, is usually assumed by the patient for these treatments. Some physicians have the patient lie on his side; more often the patient lies directly on his abdomen.

A third position, sitting, may be employed, and has certain advantages over the others. Up to the present, I have given a large number of injections with the patient seated.

Many of the patients volunteered the statement that such injections are less painful than those made otherwise. Why that should be so is difficult to say, but the situation may be analogous to the one wherein pain occasioned by a burn or trauma, as of the finger, is temporarily relieved by grasping the part and exerting pressure on it. In the sitting position the gluteal muscle is stretched, and pressure is thus indirectly exerted on the part into which the injection is made. Not only is the muscle group relaxed, but the fascia is tensed over the muscle. This tough membrane is then more easily entered than in its relatively loose state while the muscle is contracting. When the muscle is contracted, its substance becomes more spherical and hence occupies a smaller space. As the fascia over it is not contractile, it becomes relatively less distended or loose. Pinching up the skin in making a hypodermic injection decreases pain, probably because it increases the tension of the skin and allows the needle to enter more quickly and directly.

Intragluteal injections are not always given in the upper outer quadrant, which is the proper site. Sometimes the needle actually enters the region of the sciatic nerve and the large blood vessels near it. This possibility is removed when the injections are made while the patient is sitting. The patient is resting on just those parts which should not be entered. Indeed, it is difficult to enter any but the upper outer quadrant. When the patient is sitting this sector bulges and by its prominence is marked as the site for entrance, rather than the less prominent inner upper quadrant.

Not infrequently the patient, particularly a new one, attempts to grasp the needle and syringe, and patients have even broken needles by striking them suddenly while they were still in the tissues. The sitting posture, with the hands resting on the thighs, affords less chance for this, because the patient cannot as readily reach the site of the injection, at least before the physician has ample warning. Then, too, the patient is relatively immobilized, so that the site cannot as easily change its position or shape. Some patients when standing will suddenly further contract the gluteus muscle into which the injection is being made. Contrariwise, some patients contract the gluteus muscle maximally before injection and suddenly relax it at the instant the injection is made.

From the Department of Dermatology, University of Illinois College of Medicine, service of Dr. F. E. Senear.

Ordinarily it is advocated that the operator use one hand to pull the skin downward and medially from the site of the injection, inserting the needle through the taut skin. When the needle is withdrawn the skin is then released and resumes its normal position. This maneuver is supposed to lessen the possibility of escape of the injected medicament by breaking the straight line needle track. This deliberate moving of the skin prior to the injection becomes unnecessary if the patient receives his injection while sitting. The patient should stand up immediately after receiving the injection, and when he does so the sliding of the skin over the underlying muscle will automatically make the needle track discontinuous.

METHOD

The most suitable way to make these injections is to provide the patient with a stool with not too broad a seat. This allows the outer portion of the buttocks to be free and to bulge. His feet should rest on something. The height of the stool and of the footrest should be adjusted so that the knees are slightly higher than the buttocks. The patient's hands should rest on his thighs. In a clinic where large numbers of patients are treated in succession and not individually, it may be convenient to make the injections with the patients seated next to each other on a long bench provided with a footboard.

SUMMARY

The sitting posture for the patient receiving intragluteal injections is advocated, because it occasions less pain. Other advantages are mentioned, such as the lessened danger that the patient may reach the site of injection to break the needle and the impossibility of entering the region of large nerves and blood vessels.

SULFANILAMIDE TREATMENT OF SYPHILITIC INTERSTITIAL KERATITIS

Preliminary Report

I. Lewis Sandler, M.D., Washington, D. C.
Assistant Professor of Dermatology and Syphilology, Georgetown University Medical School

The purpose of this article is to report a case in which relapsing resistant syphilitic interstitial keratitis responded dramatically to sulfanilamide. I hesitate to report a single case but feel justified in the face of such a remarkable, rapid improvement of one of the most resistant and distressing of all syphilitic lesions.

I hope that this report will stimulate further controlled studies of the use of sulfanilamide in the treatment of this condition, which may occur even while the patient is under active antisyphilitic treatment.

REPORT OF CASE

F. C. S., a white man aged 28, consulted me for interstitial keratitis which had been relapsing since he was a student in his third year of high school, at which time he also had hydrarthrosis of the left knee (Clutton's joint). Since

that time at irregular intervals he had received intravenous, intramuscular and oral antisyphilitic therapy. He had had seven attacks of interstitial keratitis involving the right eye and three mild attacks involving the left eye.

When he was examined, on Nov. 2, 1936, there was a pronounced right corneal scar, with marked photophobia, lacrimation and pericorneal congestion. Typically syphilitic upper central incisors were also present. The diagnosis of syphilitic interstitial keratitis with some iritis was verified by an ophthalmologist. The patient's Wassermann and Kahn reactions were persistently positive. Examination of the spinal fluid showed it to be normal.

The keratitis improved somewhat under local therapy and continuous treatment with neoarsphenamine, silver arsphenamine, mapharsen, bismuth preparations and iodides, but seventeen months later, while the patient was still under treatment, there was a severe recurrence. Administration of foreign proteins, such as boiled skimmed milk and intravenous injections of typhoid and paratyphoid bacterin, were of no avail.

In spite of fifteen paroxysms of chills and fever from quartan malaria and in spite of all other therapy, I could not control the distressing photophobia and lacrimation.

On Oct. 24, 1938, in desperation I gave the patient an intramuscular injection of 5 cc. of prontosil (the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-2′,6′-disulfonic acid) and 10 grains (0.65 Gm.) of sulfanilamide three times daily. To my great surprise, in forty-eight hours there was a decided improvement of the conjunctival congestion, photophobia and lacrimation, and in ninety-six hours there was complete disappearance of these symptoms. At the time of this report there has been no relapse of the keratitis.

1835 Eye Street, North West.

Minor Notes

DERMATITIS VENENATA DUE TO GINKGO BERRIES

MICHAEL BOLUS, M.D., RALEIGH, N. C.

A case of dermatitis venenata due to ginkgo berries is reported because the ginkgo tree is commonly cultivated for its ornamental foliage. The seeds are covered with a soft pulplike substance which gives off a strong pungent odor. The pulp must be removed before the seeds can be used for planting. This is usually accomplished with water and a washcloth.

Webster's New International Dictionary defines the ginkgo tree as a peculiar gymnospermous tree native of eastern China, apparently preserved as a temple tree but rare in the wild state. "It is a handsome tree with fan-shaped leaves and yellow drupelike fruit." It is also called maidenhair tree or silver apricot.

REPORT OF A CASE

J. B. D., an engineer aged 29, picked some of the berries from a ginkgo tree on Nov. 6, 1938, and washed the pulp away with plain water and a wash cloth. No soap was used. On November 8 he noticed a stinging, burning sensation of the hands and eyelids, followed by edema, erythema and vesicular lesions on the lateral surfaces of the nose and the upper eyelids. He consulted an ophthalmologist, who prescribed warm boric acid compresses for the eyes. The eyelids continued to swell but did not completely close. The vesicular lesions continued to spread and on November 10 involved the dorsa of the hands and fingers and the face, neck, penis and scrotum. On November 11 the dermatitis was worse and the patient was referred to me.

A soothing zinc oxide lotion was applied to all areas except the eyelids, where the use of boric acid compresses was continued. On November 16 the vesicles had completely disappeared from all areas, leaving them dry with slight erythema and scaling. Itching was still present on the penis and scrotum. Pusey's emulsion[1] was prescribed, and all lesions had disappeared by November 19.

On November 29 a patch test was performed on the left arm with ginkgo berries, but the patch was removed at the end of two and one-half hours because of burning and stinging. The area was bright red and edematous. It was cleansed with soap and water, with alcohol and again with soap and water. The zinc oxide lotion was applied to the area, but tiny vesicles appeared in the next twenty-four hours and then rapidly subsided. Control patch tests with ivory soap and physiologic solution of sodium chloride were left on for twenty-four hours, but there was no reaction.

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1. Formula for Pusey's emulsion:

   Phenol and glycerin, each 10 minims (0.61 cc.)
   Tragacanth ½ drachm (1.94 Gm.)
   Olive oil 3 ounces (88.72 cc.)
   Distilled water to make 6 fluidounces (177.44 cc.)

VARICELLA AND HERPES ZOSTER

JOHN G. DOWNING, M.D., BOSTON

U. J., a clerk, was admitted to the Audubon Hospital on Oct. 11, 1938, for treatment of a severe contact dermatitis of both hands and forearms. He was kept in bed, and wet dressings were used constantly. On October 12 F. P. M. was admitted and placed in U. J.'s room, a small semiprivate one. The diagnosis of his condition on admission was herpes zoster of the right lower cervical segment; his temperature was 101 F., and there was a characteristic eruption.

Both patients had a normal convalescence. On October 25 U. J. complained of headache and chilly sensations, and the following morning he showed a multiform eruption on the face, scalp and extremities. A tentative diagnosis of varicella was made. He was then transferred to a contagious department of the Boston City Hospital, where on October 27 he showed a widespread eruption typical of varicella. That diagnosis was confirmed by Dr. E. Place. The patient remained at the City Hospital until November 7.

U. J. had never been vaccinated and had had no previous attack of varicella. This case shows the danger of exposing a patient who has never had varicella to herpes zoster.

News and Comment

SYMPOSIUM ON RICKETTSIAL AND VIRAL DISEASES

A symposium on the significance in public health of the viral and rickettsial diseases will be held at the Harvard School of Public Health from June 7 to 17. It will consist of a short course of lectures, clinics and demonstrations on these diseases, with special emphasis on their significance in public health. Lectures on etiology, epidemiology and methods of control will occupy five mornings. Special clinics and demonstrations will take place each afternoon. The fee for the course will be $25. Further information may be obtained by writing to the dean of the Harvard School of Public Health, 55 Shattuck Street, Boston.

DEUTSCHE DERMATOLOGISCHE GESELLSCHAFT

The fiftieth anniversary of the Deutsche dermatologische Gesellschaft will be celebrated by a meeting of the association in Breslau, Germany, from Aug. 18 to 21, 1939, under the presidency of Prof. Karl Zieler.

The main topics for discussion will be trauma in the causation of diseases of the skin, roentgen, radium and ultraviolet irradiation and the effect of climate on the treatment of cutaneous diseases.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

FALSE-POSITIVE WASSERMANN REACTIONS IN INFECTIOUS MONONUCLEOSIS. ALAN BERNSTEIN, Am. J. M. Sc. **196**:79 (July) 1938.

Transitorily positive reactions to serologic tests for syphilis were encountered in 6 of 37 cases of infectious mononucleosis. The Wassermann reaction became positive in 5; the Eagle reaction was positive in 2 and doubtful in 2 others. Since the evanescent character of such positive serologic reactions militates against the likelihood of recognition of all the instances, it is reasonable to assume that if such tests were carried out more regularly the incidence of positive reactions would be considerably higher than in the present series.

In the author's series the longest duration of a positive Wassermann reaction was nine days, but in some other cases positivity has remained much longer.

Bernstein theorizes as to the cause of this phenomenon. Because miscellaneous bacterial agglutinins are encountered in the serum of patients suffering from this disease, he regards the positive reactions as further evidence of the versatility of antibody responses in infectious mononucleosis.

UVEO-PAROTID FEVER (HEERFORDT'S SYNDROME)—NEUROLOGIC MANIFESTATIONS: REPORT OF TWO CASES. DAVID ARBUSE and MOSES MADONICK, Am. J. M. Sc. **196**:222 (Aug.) 1938.

Arbuse and Madonick report 2 instances of Heerfordt's syndrome accompanied with neurologic manifestations. In 1 a patchy erythematous eruption appeared on the face (not infrequently such an eruption involves also the arms and legs). The essential symptoms of this disease are uveitis, parotitis and a low grade chronic fever.

DISEASE AND THE NEGRO. GROESBECK WALSH and ROBERT M. POOL, Am. J. M. Sc. **196**:252 (Aug.) 1938.

Those who minister to large numbers of Negroes in practice or in clinics will be interested in Walsh and Pool's approach to the study of the differences in the diseases of white and Negro patients. These authors believe that the psychologic, emotional and personality characteristics are far more important than any anatomic or physiologic racial variations.

The following statements are illustrative of the analytic observations of the authors: The Negro "lives at peace with the various parts of his body, to an extent that is only approached in the best balanced of the whites"; and "the force of gravity seems to act with greater power upon the negro than it does upon the white."

LYNCH, St. Paul.

URTICARIA—A NEW THERAPEUTIC APPROACH. H. A. RUSK and B. D. KENAMORE, Ann. Int. Med. **11**:1838 (April) 1938.

Six persons with urticaria were treated by administration of a diet high in protein and low in sodium, with an acid ash, to which potassium chloride was added. All the patients responded satisfactorily to the treatment. The treatment is based on the assumption that in cutaneous irritability and inflammation the metabolism of potassium is altered and that an increase in potassium in the skin causes a decrease in local irritability.

READING, Galveston, Texas. [AM. J. DIS. CHILD.]

BLOOD IN THROMBOANGIITIS OBLITERANS. GRACE M. ROTH, ELIZABETH V. MACLAY and EDGAR V. ALLEN, Arch. Int. Med. **62**:413 (Sept.) 1938.

A study was made of the various components of the blood of 105 patients with thromboangiitis obliterans observed at the Mayo Clinic; 76 of the patients were gentiles and 29 were Jews. The values for serum calcium, serum protein, blood urea, serum lecithin and serum phosphorus were found to be within normal limits. In most instances the blood volume, the hematocrit value and the concentration of fatty acids and of cholesterol in the plasma were found to be normal. The authors doubt the significance of these findings, since they are inconstant in thromboangiitis obliterans.

CELLULAR CHANGES IN THE ANTERIOR HYPOPHYSES OF VITAMIN-A DEFICIENT RATS. T. S. SUTTON and B. J. BRIEF, Endocrinology **23**:211 (Aug.) 1938.

In a recent study of vitamin A–deficient rats a significant increase was found in the basophilic cells in the hypophyses. This increase was regarded as a compensatory change in the hypophysis resulting from direct damage to the gonad. Such a close relation between vitamins and endocrine structures may deserve consideration in connection with clinical studies, especially along therapeutic lines.

ON THE RELIABILITY OF PRESENT METHODS FOR CHARACTERIZING TWO GONADOTROPIC HORMONES, FOLLICLE-STIMULATOR AND LUTEINIZER. F. J. SAUNDERS and H. H. COLE, Endocrinology **23**:302 (Sept.) 1938.

Saunders and Cole report on experimental work from which they conclude that whereas it is possible to obtain from the pituitary gland two gonadotropic extracts having somewhat different effects, it is not certain that these represent two separate hormones. Whether the ovarian response shall be follicle stimulation or luteinization seems to depend also on the manner of injection and the state of the ovary. A new hypothesis is suggested as an alternative for the two hormone theory.

LYNCH, St. Paul.

GENERALIZED VACCINIA AND ECZEMA VACCINATUM. C. F. MCKHANN and R. A. Ross, M. Clin. North America **22**:785 (May) 1938.

Generalized vaccinia is the term applied to a generalized eruption following vaccination, which occurs most frequently in debilitated subjects suffering from some cutaneous disease. Eczema vaccinatum follows accidental vaccination in patients suffering from some cutaneous involvement, most commonly eczema but occasionally intertrigo, impetigo and secondary syphilis. Both types of disease are to a certain extent preventable if care is exercised in vaccinating persons predisposed to the occurrence of such complications and if those suffering from some eruption, such as eczema, are prevented from infecting themselves.

The period of incubation of generalized vaccinia varies from four to thirty days. Successive crops of lesions may occur over a period of two or three weeks.

In eczema vaccinatum the onset occurs between nine and twenty-three days after contact. While direct contact with a vaccinated area is perhaps the usual mode of infection, experimental evidence has been offered showing the possibility of droplet infection. Vaccine virus has been isolated from the throats of vaccinated persons on the fourth and fifth days *post vaccinatum*. After infection, an exacerbation of the underlying cutaneous disease usually precedes the characteristic eruption. Rarely do the lesions remain limited to the previously injured areas of skin.

The course of both of these conditions is usually mild, although there may be several considerable elevations of temperature lasting from seven to ten days. Occasionally the cutaneous lesions may assume the severity and gravity of malignant variola.

While these diseases are not of frequent occurrence, only under exceptional circumstances is it advisable to vaccinate a debilitated person suffering from a cutaneous disease, acute or chronic, or from an acute or debilitating disease. The

infant and the young child with eczema should also be carefully guarded from contact with recently vaccinated persons.

EUGENE H. SMITH, Ogden, Utah. [AM. J. DIS. CHILD.]

RECENT ADVANCES IN LEPROSY, AND THE METHODS ADOPTED FOR DEALING WITH THE PROBLEM IN FRANCE. CHARLES FLANDIN, Brit. J. Dermat. **50**:399 (Aug.-Sept.) 1938.

In this, the fifth Prosser White oration, Flandin reviews the situation in general with regard to leprosy, as it was considered at the recent congress in Cairo, Egypt. He discusses leprosy from the standpoint of epidemiology, contagiousness, symptomatology, allergy, classification, bacteriology, experimental inoculation and treatment. One difficulty is the impossibility of determining accurately the duration of incubation in leprosy. This is so because one is not sure that the cutaneous or neurologic symptoms are the first signs of the disease. Flandin believes that in many cases it begins with fever—fever that may be continuous or oscillating or like that in malaria. In these cases the fever responds only to specific antileprous treatment, rather than to the usual antipyretic therapy. He has noted in some cases the presence of pain, either neuralgic or neuritic, localized to a definite nerve area or spread to various parts of the body. These attacks may be painful and last for months; and Flandin considers these symptoms of pain and fever which may precede recognizable leprosy manifestations of an allergic response to the disease. When he is unable to find Bacillus leprae on section, he injects chaulmoogra oil intradermally, and on the sixth or eighth day there appears an inflamed area from which numerous bacilli can be recovered. He reports that the consensus at the congress was that treatment with chaulmoogra preparations was still the best method, and he himself has had excellent results from intravenous injections of a colloidal suspension containing 3 per cent of chaulmoogric extracts.

ON THE QUESTION OF THE ETIOLOGY OF PEMPHIGUS VULGARIS AND DERMATITIS HERPETIFORMIS (DUHRING'S DISEASE): A CLINICAL EXPERIMENTAL STUDY. A. DOSTROVSKY, I. GUREVITCH and H. UNGAR, Brit. J. Dermat. **50**:412 (Aug.-Sept.) 1938.

The authors discuss their experiments, the results of which seem to indicate that some filtrable virus belonging to a group of neuropathic viruses produces pemphigus vulgaris and dermatitis herpetiformis, and that both diseases belong to the same group.

The experiments were performed on 135 rabbits, which received intracisternal, intracerebral and intravenous injections of vesicular fluid, blood serum and cerebrospinal fluid obtained from patients with both diseases. In a certain number of the rabbits an infection of the central nervous system developed, producing complete paralysis of the posterior and, later, of the anterior extremities, or only paresis of the extremities. In some of these there was encephalomyelomeningitis. The experiments were apparently carefully controlled and are fully discussed.

MATCH AND MATCH-BOX DERMATITIS. ROBERT KLABER, Brit. J. Dermat. **50**:451 (Aug.-Sept.) 1938.

Klaber himself suffered from matchbox dermatitis, which stimulated his interest to the point where he made a thorough study of the matchbox industry, and his account of it is interesting. He has determined that the dermatitis is due to phosphorus in the form of phosphorus sesquisulfide.

DERMATOMYOSITIS AND POIKILODERMA ATROPHICANS VASCULARE: A CLINICAL AND HISTOLOGICAL COMPARISON. G. B. DOWLING and W. FREUDENTHAL, Brit. J. Dermat. **50**:519 (Oct.) 1938.

From descriptions in the literature it is sometimes difficult to distinguish between dermatomyositis and poikiloderma. The contrast is striking, however,

when the two diseases are seen side by side. The authors accept John Lane's case as an instance of characteristic poikiloderma atrophicans vasculare. In this condition the face is often spared. The eruption is made up of a number of elements, namely, telangiectases, tiny petechiae, pigmentation, depigmentation and miliary lichenoid scaly papules. The lesion is generally covered with adherent scales. The skin is atrophic and pleated in places. There is no sclerosis. The lesions may be variegated or evenly distributed; closely set and reticular, or arranged in meshes enclosing areas of normal, erythematous or atrophic skin. Occasionally ulcers or scars of ulcers are seen. There are no systemic symptoms other than slight subjective sensations from the cutaneous changes. The disease is slowly progressive.

In dermatomyositis there is a more regular march of events. The earlier symptoms are swelling of the eyelids and face and sometimes of other parts of the skin. Gradually muscular changes develop, consisting of loss of volume and hardness, and in later stages contractures. By degrees the skin becomes the seat of sclerous, pigmentary and vascular changes, the epidermis becoming harsh and scaly. There is progressive weakness in most cases. The histologic changes are equally striking. Contrasting points, both clinical and histologic, are well illustrated in tabular form, and the article has excellent illustrations in color.

RATTNER, Chicago.

PULMONARY LESIONS IN ANIMALS PRODUCED BY VIRUS OF LYMPHOGRANULOMA INGUINALE. E. VON HAMM and RALPH HARTWELL, J. Trop. Med. **40**:213 (Sept. 15) 1937.

Intrapulmonary injections of tissue emulsions containing the active virus of lymphogranuloma venereum produce different effects in rabbits, guinea pigs and mice. In rabbits, the reaction in the lung is nonspecific and appears in control animals given injections of virus-free emulsions and of inactive virus. The proliferation of the endothelial cells is only slightly noticeable. In white mice, no characteristic changes are produced. Antigens prepared from the treated lungs of the various animals do not produce a positive Frei reaction in patients suffering from lymphogranuloma venereum.

PELLAGROID BERIBERI. ALDO CASTELLANI, J. Trop. Med. **41**:294 (Sept. 15) 1938.

In countries where beriberi and pellagra are endemic, cases are encountered in which, in addition to the beriberi symptoms, cutaneous lesions of pellagra are found. The condition is termed pellagroid beriberi by the author, who states that in this instance the term pellagra is used to indicate not only the typical cutaneous lesions of pellagra but other changes, especially keratosis pilaris of the type found in A avitaminosis (phrynoderma). When the condition is typical, the following features are present: (1) weakness and paresis of the lower extremities, loss of knee jerks, stepping gait and patches of anesthesia or hyperesthesia; (2) chronic roughening and pigmentation of the skin of the exposed parts and at times of the perianal region and other unexposed areas and possible stomatitis; (3) follicular, papular eruptions.

The syndrome is due to a pluriavitaminic deficiency and if treated early responds to a diet rich in the various vitamins. LAYMON, Minneapolis.

DESENSITIZING EFFECT OF *l*-ASCORBIC ACID (VITAMIN C). G. DAINOW, Ann. de dermat. et syph. **6**:830 (Sept.) 1935.

According to Dainow, studies on the use of *l*-ascorbic acid in the treatment of allergic diseases have shown that it has considerable desensitizing power, and he believes this will be borne out by future investigation. He reports 5 cases of arsphenamine dermatitis treated with it, and from the good results obtained in these cases he concludes that *l*-ascorbic acid will supersede sodium thiosulfate as the best medicament for this condition.

KERATOSIS NIGRICANS: TINEA NIGRA. F. SILVA, Ann. de dermat. et syph. **6**:928 (Oct.) 1935.

The author concludes that tinea nigra (Castellani, 1905) is identical with the condition described by Cerqueira in 1891 and called keratomycosis nigricans palmaris, because the lesions seem to be the same in all cases, and a cladosporium fungus is the causative organism in both. The only difference is the location of the lesions. The name tinea nigra should be used, he thinks, because it covers all sites and will still be applicable if another fungus is found to be the cause in some future cases. The disease begins with little black dots, which gradually coalesce to form larger spots. The lesions vary in size, are smooth, nonelevated and nonitchy and disappear and reappear, but on the whole steadily increase in number. The color sometimes becomes lighter in the evolution of the disease. All ages and both sexes are affected, the disease predominating in the white race and in halfbreeds. Transmission seems to be by direct contact. In differential diagnosis a number of diseases are to be considered, namely: pigmented nevus, Addison's disease, epidermal blastomycosis, tinea versicolor, tinea nigrocircinata, and erythematopigmentary dermatosis of Freund. Many medicaments have been used, including sulfur, resorcinol, salicylic acid in alcohol and weak solution of iodine.

URTICARIA WITHOUT URTICARIAL SYMPTOMS. P. CHEVALLIER, Ann. de dermat. et syph. **7**:113 (Feb.) 1936.

Urticaria occurs in two clinical forms—the usual wheal-like type and massive edema of the subcutaneous tissues (angioneurotic edema). It may be due to local irritation by some agent in the patient's environment or to some internal toxic agent's producing manifestations on the skin. The latter type is considered in this article. It may produce either clinical form of the disease. Urticaria is really a disease complex. Urticarial swelling may occur in any part of the body, including all organs, wherever loose connective tissue exists. Migraine, epilepsy and other diseases involving the nervous system have been explained on the basis of angineurotic edema. Involvement of the mucosa of the bladder or the urethra may produce anuria or hematuria. Other examples of visceral urticaria are paroxysmal tachycardia due to involvement of the heart, and pulmonary edema. Urticaria has always been considered a disease of the skin, but actually it is a systemic disease which may or may not be accompanied with cutaneous manifestations. Gastroscopic examinations have been particularly useful in showing that there is a purely visceral form of urticaria, for by this means the ordinary urticarial lesions and massive edema can actually be seen.

GANDY, Houston, Texas.

CHRYSOCYANOSIS: CUTANEOUS PIGMENTATION AFTER INJECTION OF GOLD SALTS. F. CARDIS and M. CONTE, Ann. de dermat. et syph. **7**:229 (March) 1936.

Cardis and Conte consider chrysocyanosis a new disease characterized by uniform and persistent pigmentation on the exposed surfaces and due to the deposition of gold in the skin. The series they studied consisted of 34 patients under treatment for tuberculosis with injections of gold salts. In most cases the pigmentation appeared two or three years after gold therapy. It is described as beginning usually around the eyes and on the lids, spreading later over the forehead, stopping at the hair line; in some patients it involves the forearms and the backs of the hands, but it is usually limited to the face. This masklike pigmentation is accompanied by no symptoms, being only a cosmetic defect. It may be confused with argyria, but the latter condition has a distinct gray tint which should make the differentiation easy. Histologic study shows the deposit of grains of metallic gold in the skin, blood vessels and lymphatic vessels. There is no known treatment for the condition.

URTICARIA WITH ATROPHIC GASTRITIS. P. CHEVALLIER and F. MOUTIER, Ann. de dermat. et syph. **7**:337 (April) 1936.

The authors state that there are two kinds of chronic urticaria, namely, urticaria of digestive and urticaria of nondigestive origin. The digestive type is practically always accompanied with some degree of atrophic gastritis, which may be improved and in many cases cured by administration of iron. Atrophic gastritis, as evidenced by gastroscopic studies, was found in more than half the authors' cases. Hydrochloric acid may be present in normal or slightly subnormal amount if the atrophic gastritis is not severe; occasionally a normal gastric mucosa may be present with achlorhydria. In the latter cases the eosinophil count is within normal limits, whereas in urticaria without participation of the digestive organs a certain degree of eosinophilia is the rule. The dose of iron given begins at 3 Gm., and is gradually increased to 6 Gm. The medication should be continued for a long time to prevent recurrences. Hydrochloric acid should be taken concurrently to prevent interference with the digestive function. It is claimed that iron benefits the urticaria directly, in addition to its general effect on the patient.

GANDY, Houston, Texas.

ACUTE LUPUS ERYTHEMATOSUS LIMITED TO THE FINGER. J. GATÉ, P. CUILLERET and P. MOREAU, Bull. Soc. de dermat. et syph. **45**:481 (April) 1938.

A girl aged 18 entered the hospital in December 1937, complaining of an eruption which had appeared the previous September. Although the lesions were limited to the dorsal surfaces of the fingers, a diagnosis of lupus erythematosus was made after clinical and histologic study. On account of fever and albuminuria the condition was classified as acute.

IMPETIGINOUS STOMATITIS. J. NICOLAS, J. ROUSSET and J. RACOUCHOT, Bull. Soc. de dermat. et syph. **45**:499 (April) 1938.

The authors call attention to pyogenic stomatitis associated with impetigo. Three cases in the same family were cited. The use of 1 per cent methylthionine chloride (methylene blue) and 10 per cent silver nitrate resulted in rapid improvement.

LYMPHOGRANULOMATOUS CHANCRE. A. SÉZARY and H. MASCHAS, Bull. Soc. de dermat. et syph. **45**:574 (April) 1938.

The patient, a man aged 52, first noted a penile lesion in September 1937. At the time of observation, in January 1938, there was an ulcerated lesion about 1.5 cm. in diameter involving the glans and prepuce. The inguinal and iliac nodes were enlarged. The intradermal reaction for chancroid was negative; the Frei reaction was positive. Serologic tests for syphilis gave negative results. The case was noteworthy on account of the ulcer, which gave rise to a clinical picture resembling a malignant neoplasm.

TREATMENT OF SYCOSIS BY THE INTRAVENOUS INJECTION OF LUGOL'S SOLUTION. A. TZANCK and S. LEWI, Bull. Soc. de dermat. et syph. **45**:584 (April) 1938.

The 2 patients discussed by the authors were suffering from long-standing sycosis of the beard, which had resisted various forms of therapy. Remarkably rapid improvement was obtained by intravenous injection of compound solution of iodine.

TREATMENT OF NICOLAS-FAVRE DISEASE WITH SULFANILAMIDE. L. R. MONTEL and NGUYEN-VAN-THO, Bull. Soc. de dermat. et syph. **45**:652 (April) 1938.

In 3 cases of recently acquired Nicolas-Favre disease, treatment with sulfanilamide resulted in complete regression in forty-nine, forty-eight and twenty-five days. In a case of anorectal syndrome no result was obtained with the same type of therapy.

TREATMENT OF LUPUS TUBERCULOSIS IN THE LABORATORY OF FINSENTHERAPY OF ST. LOUIS IN 1937. JEAN MEYER, Bull. Soc. de dermat. et syph. **45**:804 (May) 1938.

The author presents statistics concerning 305 cases of lupus vulgaris observed during 1937, 134 of recently acquired and 171 of long-continued infection. Of 89 patients in the former group who were regular in their treatment, 45 were healed, 19 by surgical intervention and 26 by application of Finsen light. Twenty-one other patients were still under intensive therapy and were progressing satisfactorily. The remaining 23 had severe involvement, but healing seemed at least probable. In 30 cases the disease was regarded as incurable, in all being of many years' duration. During the year 7 cancers were treated, 5 of which appeared within areas of radiodermatitis.

Relapses were rare when apparently entire healing had been produced by surgical excision but were relatively frequent after treatment by scarification, curettage or ultraviolet irradiation. In 73 per cent of cases the onset was before the age of 30 years.

THE STOMACH IN NEURODERMATITIS. P. CHEVALLIER, F. MOUTIER, LEMELAND and LACOUR, Bull. Soc. de dermat. et syph. **45**:863 (May) 1938.

The authors report the results of gastroscopic study and gastric analysis in 3 cases of subacute disseminated neurodermatitis and 4 cases of circumscribed neurodermatitis. No significant abnormalities were noted.

LAYMON, Minneapolis.

CUTANEOUS MANIFESTATIONS IN RHEUMATIC FEVER. D. CORREA and O. MACCIO, Arch. de pediat. d. Uruguay **8**:752 (Dec.) 1937.

In 500 cases of rheumatic fever, Correa and Maccio five times observed the erythema of Besnier; in 4 of these cases the erythema coincided with cardiac involvement. One of the children died as a result of the rapid evolution of the erythema.

They also encountered 4 cases in which there were subcutaneous nodules, in 3 associated with cardiac involvement. Nodular erythema was found in a single case.

RITTER'S DISEASE AND PEMPHIGUS NEONATORUM. E. PELUFFO and A. RAMÓN GUERRA, Arch. de pediat. d. Uruguay **9**:233 (April) 1938.

An epidemic of pemphigus neonatorum developed in the obstetric clinic of the Russel-Pereira Hospital, Montevideo, Uruguay. The prognosis was good, the only complications being local infections forming pyoderma. In only a single infant did the disease take a malignant course, with development of marked exfoliation, purpura and generalized epidermolysis (Ritter's disease). This infant died five days after the onset.

SCHLUTZ, Chicago. [AM. J. DIS. CHILD.]

AVITAMINOTIC EDEMA OF INFANCY. CHAVARRÍA, A. PEÑA and WERNER ROTTER, Rev. méd. latino-am. **23**:1027 (June) 1938.

This condition, hitherto rare, was observed in 43 children, or 1 per cent of admissions to pediatric hospitals in Costa Rica in less than three years. Most of the children came from poverty-stricken insanitary homes in the city, and 31 of them were less than 5 years of age. The clinical picture was more or less similar in all instances; the children were apathetic, wretched and undernourished and cried out in pain when moved; some had photophobia; anorexia was extremely common; those who could walk had a swaying or spastic gait; mucous diarrhea was almost universal. There was a variable amount of edema of the feet, hands and face and in some cases generalized anasarca. The mucous membranes of the

mouth were red, with pallid streaks resembling atrophy, and at the oral commissures were heaped-up erosions. The tongue was smooth and red; the hair was dry and silky and was coming out in bunches. The skin of the hands and feet, in the early stages, was smooth and of a reddish or cyanotic hue, which diminished gradually as it progressed upward but lacked completely any sharp line of demarcation. The skin was cold. After the acute phase had passed, the skin in these areas desquamated, became pigmented and at times showed vesicles and bullae. More rarely, there were indolent ulcers and hemorrhagic lesions.

Of the 43 patients studied, 17 died, but these were practically moribund on admission; the cause of death in most instances was intercurrent pneumonia or bronchopneumonia. At autopsy one observed, in addition to the lesions already noted, fluid in the body cavities, atrophic colitis and fatty changes in the liver.

When the condition is favorable, the response to dietary therapy is amazingly rapid; the diet consists chiefly of milk, cereal gruels, cod liver oil and orange juice.

The authors conclude that the condition is a true avitaminosis, corresponding to incipient beriberi and pellagra, with (in some cases) an element of scurvy. They note that its increase is coincidental with the economic depression. They note the similarity to the condition called erythredema but feel that the response to diet justifies the appellation of avitaminotic edema. LEIFER, New York.

EXPERIMENTAL OBSERVATIONS ON THE FAT METABOLISM IN PSORIASIS VULGARIS. HEINZ HERING, Dermat. Wchnschr. **106**:80 (Jan. 15); 109 (Jan. 22) 1938.

Hering reviews briefly the literature in regard to changes of fat metabolism in psoriasis. He determined the values for total fat, total cholesterol, cholesterol esters and phosphatide phosphorus in 51 cases. The determinations were made during fasting and also four, eight and twenty-four hours after ingestion of a test meal of olive oil and cholesterol. The patients included 11 with normal skin, 17 with psoriasis and 18 with eczema. The average value for total fat of the patients with psoriasis was somewhat higher than normal, but some of the values were below the normal average. The lipoid content of the serum and the metabolism curve were redetermined after the psoriasis had cleared in 4 instances. The findings did not change materially. The author concludes that the evidence is not sufficient to indicate that psoriasis is due to an abnormality of fat metabolism.

NAEVUS VARICOSUS ET ANGIOMATOSUS (ACROSARCOMA KAPOSI). K. H. VOHWINKEL, Dermat. Wchnschr. **106**:125 (Jan. 29) 1938.

A milkman 17 years of age presented a group of dome-shaped nodules on his right leg. They varied in size from that of a grain of pepper to that of a bean and were violet-brown. The consistency was rubbery. Elsewhere on the leg were varices and a number of pigmented scars. The condition had first appeared four years previously. Histologic examination showed a normal epidermis. In the corium were groups of capillaries with a fibrous stroma and areas of pigment (hemosiderin). The author considers this condition to be closely related to Kaposi's sarcoma, if not an unusual form of that lesion.

THE CAUSATIVE ORGANISM OF LYMPHOGRANULOMA VENEREUM. N. MELCZER, Dermat. Wchnschr. **106**:128 (Jan. 29) 1938.

Melczer discusses previous reports of the demonstration of elementary bodies in material from patients and animals with lymphogranuloma venereum. He describes a modification of previously used methods. Photomicrographs of material from various sources are reproduced.

ALTERATION OF THE COLOR OF THE HAIR BY EXTERNAL INFLUENCES. HANS JÄRNECKE, Dermat. Wchnschr. **106**:212 (Feb. 19) 1938.

The author describes a patient in whom a greenish discoloration of the hair developed. Chemical and spectroscopic investigations showed the presence of copper in the hair; the source of the metal was copper hairpins.

THE LOCALIZATION OF HERPES ZOSTER. P. BERGGREEN and E. G. SCHÜLER, Dermat. Wchnschr. **106**:216 (Feb. 19) 1938.

The authors reviewed 2,014 cases of herpes zoster observed between 1920 and 1935. The most frequently involved nerve roots were the trigeminal and the third cervical. Males were somewhat more frequently affected than females. The right and left sides were about equally involved.

TAUSSIG, San Francisco.

PRIMARY TUBERCULOSIS OF THE VULVA, IN ASSOCIATION WITH ERYTHEMIA NODOSUM. A. NORDENSKJÖLD, Acta pædiat. **20**:257, 1937.

Accumulated clinical experience indicates that the tubercle bacillus rarely invades the body through the skin or through the mucous membranes; these serve as the portal of entry in probably not more than 0.1 per cent of all cases. A limited number of cases have been reported in which the primary focus was located in the skin, the tonsil, the gum or the middle ear of an infant. Although infection of the male genital organ during ritualistic circumcision is by no means rare, the occurrence of a primary focus in the vulva appears to be exceedingly uncommon. Approximately 11 authentic cases of this phenomenon have been reported; in 10 instances the patient was an infant or a child. The diagnosis is usually difficult, and the source of the infection generally evades unequivocal detection.

Nordenskjöld describes what she regards as the first case to be published in Sweden. The patient was a 6 year old girl who entered the hospital because of a week's illness, which consisted of fatigue, swelling of the lymph glands of both groins and fever. The nodes were found to be slightly enlarged, tender, matted together and adherent to the overlying skin, which was reddened and edematous. There were lesions characteristic of erythema nodosum. A purulent vaginal discharge was present. The Hamburger tuberculin test gave positive results, and the sedimentation rate of the erythrocytes was considerably accelerated. A few days after admission the vulva became conspicuously inflamed, and a small ulcer appeared near the orifice of the urethra. These manifestations subsided within a week; the lymphadenopathy receded without suppuration. Direct smears of the discharge from the vulva failed to aid diagnosis, but pus from the ulcer produced tuberculosis in guinea pigs, and tubercle bacilli of the human type were cultivated from the discharge. Treatment was limited to local hygienic measures. Four months later the local lesion had almost disappeared, and eighteen months after the beginning of the illness the patient was entirely well. Roentgen examination of the chest yielded negative findings; no tubercle bacilli were demonstrated in material obtained by gastric lavage. The correctness of the diagnosis in this case, as in others, is supported by (1) the character of the ulceration, (2) the subsequent appearance of tuberculous lymphadenitis of the regional nodes, (3) the appearance of erythema nodosum in chronologic association with the lesion and (4) the absence of evidence of tuberculous infection in other parts of the body. The bibliography is helpful.

MCCUNE, New York. [AM. J. DIS. CHILD.]

Society Transactions

MINNESOTA DERMATOLOGICAL SOCIETY

LOUIS A. BRUNSTING, M.D., *President*

Duluth, July 31, 1938

F. W. LYNCH, M.D., *Secretary*

Exfoliative Dermatitis with Lymphatic Leukemia. Presented by DR. F. T. BECKER and DR. M. A. NICHOLSON, Duluth, Minn. (by invitation).

Mrs. O. M., aged 49, first had a pruritic papular eruption in the spring of 1934. At that time no diagnosis could be made. Physical examination showed an elevation of blood pressure to 170 systolic and 90 diastolic. Renal glycosuria was present and was controlled by diet. At this time the white blood cell count was 6,000 per cubic millimeter. The differential count showed polymorphonuclear leukocytes, 55 per cent; large lymphocytes, 14 per cent; small lymphocytes, 18 per cent; monocytes, 3 per cent; eosinophils, 6 per cent, and immature lymphocytes, 4 per cent. The dermatitis persisted without a great deal of change.

In November 1935 the gallbladder was removed. During convalescence thrombophlebitis developed. The cutaneous eruption became progressively worse and nearly universal. Just prior to menstruation the skin would become erythematous, much more edematous and pruritic. At the end of twenty-four hours the skin would exfoliate in large sheets. This would last three or four days, after which the swelling would subside, leaving orange-red patches of dermatitis. Because of the apparent relation to menstruation, a castration dose of high voltage roentgen therapy was given in the spring of 1937. There was slight improvement in the dermatitis for several months, but the periods of exacerbation have returned once or twice a month, usually about the first and the fifteenth.

During the past three months the patient has received high voltage roentgen therapy (200,000 kilovolts; 8 milliamperes), 200 roentgen units (r) filtered through 1 mm. of copper to the regional lymph glands and the splenic area. Also, 360 roentgen units has been given to the involved skin in fraction doses of 90 r. This has been given with the machine for superficial therapy (100 kilovolts; 5 milliamperes) and no filtration. Locally, she has used camphor in oxycholesterol. During the attacks she has taken a considerable amount of pentobarbital sodium, but the exacerbation starts before she takes the sedative.

Large patches of slightly scaly orange-red dermatitis are present on the face, neck, trunk and extremities. There is generalized lymphadenopathy; the spleen cannot be palpated. In the periods of exacerbation the skin becomes erythematous and edematous for several days, after which it exfoliates, leaving an area which is only slightly scaly and is orange-red.

Histologic section of a cervical lymph node revealed hyperplasia, according to Drs. E. T. Bell and G. L. Berdez. A section of the bone marrow showed a picture within normal limits.

The hemoglobin content of the blood was 96 per cent. The red cell count was normal. The leukocyte count was 14,000 per cubic millimeter. The differential count showed: polymorphonuclear leukocytes, 23 per cent; myeloblasts, 9 per cent; large lymphocytes, 18 per cent; immature lymphocytes, 45 per cent; monocytes, 4 per cent, and eosinophils, 1 per cent. The blood smears have been studied by Drs. W. D. Coventry and Hal Downey, who have both and separately reached the same conclusions: (1) that they have never seen blood like this, (2) that many of

the lymphocytes are immature but that the immaturity is unlike that seen in ordinary lymphatic leukemia, suggesting, rather, origin from the reticuloendothelial system, and (3) that this blood shows leukemic reticuloendotheliosis in which differentiation is along lymphatic lines.

Histologic preparations of several specimens of skin are shown.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn. (written report after examination of sections): The sections of skin strongly suggested to me the diagnosis of monocytic leukemia of Schilling. Dr. C. H. Watkins made a diagnosis of leukemic reticuloendotheliosis, there being reticular cells going over into lymphocytes without going through the stem cell stage. After biopsy of a lymph gland Dr. A. C. Broders made a diagnosis of lymphosarcoma.

Dr. Watkins and I reported a case of monocytic leukemia in which the blood picture at one time was that of the Schilling type of monocytic leukemia and at another time was that of lymphatic leukemia. Your case illustrates the close interrelation between the various types of lymphoblastoma. When the patient was shown in Chicago, at which time only Dr. Downey's report on the blood was available, I pointed out the similarities of the clinical changes in monocytic leukemia and mycosis fungoides.

A Case for Diagnosis (Sarcoid? Lupus Miliaris Disseminatus?). Presented by DR. CARL LAYMON, Minneapolis.

A. K., a white woman aged 26, first noted an eruption on her upper lip in December 1937. A short time later lesions appeared on the cheeks and chin. In February 1938 similar papules were noticed on the knees and on the backs of the hands.

The eruption consists of faint bluish red papules 1 to 3 mm. in diameter, located on the cheeks, the chin, the dorsa of the hands and to a less extent the knees. The blood smears show no evidences of leukemia. The Mantoux test (1:1,000 dilution of tuberculin) was negative on two occasions, in May and July 1938.

The changes seen histologically in sections from a lesion on the hand consisted of nests of epithelioid cells and lymphocytes in the cutis. In sections from a lesion on the chin there were giant cells in addition to the other features. No caseation necrosis was seen.

DISCUSSION

DR. CARL LAYMON, Minneapolis: Physicians who have seen this patient previously have agreed that the most likely diagnosis is either sarcoid or lupus miliaris disseminatus. The repeatedly negative reactions to tuberculin (1:1,000) favor the latter possibility. The histologic observations did not permit a clearcut differentiation, the sections from lesions on the hands favoring sarcoid and those from the nodules on the face favoring lupus miliaris disseminatus. As yet, roentgenograms of the chest and bones have not been taken. These may be of help in making a final diagnosis.

Naevus Epitheliomatocylindromatosus. Presented by DR. M. A. NICHOLSON and DR. F. T. BECKER, Duluth, Minn. (by invitation).

E. M., a white man aged 44, first had tumors on his scalp in 1915. There have been a progressive enlargement and an increase in the number of new growths during the ensuing years. Several have been removed surgically.

General physical and laboratory examinations, including Wassermann and Kline tests of the blood, gave essentially negative results. On the scalp are numerous reddish blue tumors varying in size from that of a walnut to that of a small hen's egg. They are putty-like in consistency and freely movable.

Histologic sections of one of the tumors are presented.

DISCUSSION

DR. CARL LAYMON, Minneapolis: This is an unusually good example of cylindroma. A case characterized by lesions on the trunk was reported about a year ago in the German Archives (Schuermann and Weber). The authors also mentioned the genitals and extremities as other infrequent localizations.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: This is a classic example of turban tumor, and the presence of the discrete lesions on the trunk is noteworthy. In some cases of this type lesions are found on the trunk and extremities when the process is widespread and of long standing.

Hydroa Aestivale. Presented by DR. GEORGE C. DOYLE, Duluth, Minn.

H. H., a white youth aged 18, has an eruption on his face and forearms which began at the age of 8 years. He states that the eruption began on his face in the spring, that he has had it each spring since and that it usually disappears late in the summer or in the fall; that in the summer of 1937 it was present all summer and has been present at intervals during the past winter. The eruption consists of bullae, vesicles, excoriations crusts and scars on the nose, the cheeks, the ears and the extensor surfaces of the forearms.

DISCUSSION

DR. F. T. BECKER, Duluth, Minn. (by invitation): I have had an opportunity of studying this case rather thoroughly. Dr. Cecil Watson, of the University of Minnesota, was unable to find coproporphyrin, and normal amounts of uroporphyrin were present. When I was at the university I also studied a case of Dr. Rusten's in which the erythema time with ultraviolet rays was very high. On the other hand, a patient with xeroderma pigmentosum showed a blistering reaction after exposure to rays of from 2,700 to 3,300 angstrom units after a very short interval.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: The character and distribution of the eruption show a definite reaction of hypersensitivity to light. It is a difficult problem in each case to settle the question of which region of the spectrum is involved in the production of the dermatosis. Recent evidence indicates that there is no relation between the syndrome of hypersensitivity to light and disturbances in porphyrin metabolism in such cases.

Scleroderma Diffusum and Chronic Discoid Lupus Erythematosus. Presented by DRS. M. A. NICHOLSON, K. W. EMANUEL and F. T. BECKER (by invitation).

Mrs. G. J., a white woman aged 30, of Finnish descent, first had lupus erythematosus about ten years ago, and for this condition she has received numerous injections of gold salts intravenously, as well as some intramuscular injections. In the spring of 1937 she first noticed an increase in the pigmentation of the extremities and a thickening of the skin of the arms and hands. The condition has become progressively worse, spreading to most of her body, and her fingers have become stiff.

General physical examination gave essentially normal results. The blood pressure was 110 systolic and 76 diastolic. Roentgenograms of the chest showed some calcified hilus glands and also a few calcified parenchymal lesions. Roentgen study of the abdomen showed calcification in the vicinity of the adrenal glands.

The calcium content of the blood was 9.85 mg. per hundred cubic centimeters, and the chloride content varied from 482 to 498 mg. per hundred cubic centimeters of plasma. The basal metabolic rate was +11 per cent. The hemoglobin content was 79 per cent, with 4,100,000 red blood cells. The white blood cell count was 7,700. The differential count was normal. The Wassermann and Kline reactions of the blood were negative.

There is a masklike facies. Over the nose and both cheeks is an erythematous plaquelike eruption with atrophy and scaling, typical of chronic discoid lupus

erythematosus. There is rather generalized hyperpigmentation, more pronounced on the extremities but present in irregular patches on the trunk. The skin of the extremities feels indurated and stiff; that of the trunk is also involved in large areas, with small irregular pieces of normal skin between. Sclerodactylia is present in the hands and to a lesser degree on the feet.

DISCUSSION

DR. F. T. BECKER, Duluth, Minn. (by invitation): This is a rather interesting and unusual clinical combination. The patient presents a rather diffuse hyperpigmentation of the skin. The mucous membrane is entirely free of pigment. She also has hypotension, but a salt-free diet produced no exacerbation of her general weakness. Interestingly enough, she also shows calcification in the region of the adrenal glands, and several internists have considered Addison's disease as a strong possibility.

PHILADELPHIA DERMATOLOGICAL SOCIETY

THOMAS BUTTERWORTH, M.D., *Chairman*

Sept. 16, 1938

HERMAN BEERMAN, M.D., *Secretary*

Lymphadenosis Cutis Circumscripta. Presented by DR. JOHN B. LUDY.

M. F., a white woman aged 62, noticed in June 1937 a reddish pink area on her forehead, a little to the right of the midline. This gradually increased by the addition of similar lesions to the right and below. Trauma did not seem to play a part in its causation. There were slight itching and scanty scaliness. She now presents a patch of violaceous rounded moderately infiltrated papules and nodules with an ill defined tendency to grouping, practically confined to the right side of the forehead; many are telangiectatic. Histologic sections suggested cutaneous aleukemic lymphoid leukosis, but a monocytic type was by no means excluded. The Wassermann and the Kahn test were negative. A blood count showed 85 per cent hemoglobin, 4,680,000 red blood cells and 13,800 white blood cells, with 62 per cent polymorphonuclear leukocytes, 33 per cent lymphocytes, 2 per cent monocytes and 3 per cent eosinophils.

DISCUSSION

DR. FRED D. WEIDMAN: I overheard a number of the members discussing this case, stating that the lesion looked like sarcoid. Against this, I agree with the diagnosis as presented, but only to the extent that the patient does not have sarcoid of Boeck. The lesion can still be closely related to one of the other types of sarcoid, such as the Spiegler-Fendt type, which has been relegated lately to the blood-forming group. In the histologic sections there were, in addition to the lymphocytes, large clear cells which the pathologist noted in his pathologic report and suggested might be monocytes. This makes one think, too, of the possibility of Hodgkin's disease, but I saw no multinucleated forms. Since the patient has not had generalized lymphadenopathy, the safest diagnosis to advance is Spiegler-Fendt sarcoid.

DR. JOHN B. LUDY: I feel that the patient has leukaemia cutis. When I first saw her I thought the eruption looked like Riehl's melanosis, but the pathologist states that it is leukaemia cutis.

Urticaria Pigmentosa. Presented by DR. JOHN B. LUDY.

E. McD., a white woman aged 32, has pigmented macules the size of a finger nail which developed after sunburn eight years ago. The lesions are limited to

the arms, neck and back. Itching is present, and on massage the lesions become elevated and redder and take on urticarial characteristics.

DISCUSSION

DR. CARROLL S. WRIGHT: The members will recall the woman I presented last May (ARCH. DERMAT. & SYPH. **39**:383 [Feb.] 1939), whose lesions were similar to these. The present lesions are smaller than it is customary to see in urticaria pigmentosa in children, but I believe that if this case is diagnosed as one of urticaria pigmentosa, the other certainly should have been for the type of lesion is exactly the same.

DR. SIGMUND S. GREENBAUM: I think this condition is simply more marked urticaria pigmentosa than that in the case presented last year by Dr. Wright. In the adult type the lesions have a tendency to appear simply as pigmented macules, as this woman's have. I think this patient presents the adult form of urticaria pigmentosa.

Sarcoid of Boeck. Presented by DR. JOHN B. LUDY.

G. M., a Negro aged 29, noticed an eruption on his right thumb three years ago. After a year an injury apparently activated the process, and lesions appeared on the lips, nose and left knee. Recently some have developed on the back of the right shoulder. All the lesions are painful. The eruption consists of grouped or occasionally single tender brownish red moderately firm papules, which have recently become flattened. The Wassermann and the Kahn test were reported negative on April 13, 1938. A histologic diagnosis of sarcoid of Boeck was made by Dr. C. F. Geschickter, of the Johns Hopkins Hospital.

DISCUSSION

DR. H. J. SMITH: Clinically the eruption looks like sarcoid of Boeck.

DR. FRED D. WEIDMAN: I did not see the patient, but I saw the section of the lymph node, which is good for sarcoid of Boeck. The diagnosis of Schaumann's disease may also be considered, in view of this picture, and inquiry should be made into the condition of the lungs by means of roentgenograms and into the matter of cystic disease of the small bones of the hands and feet.

DR. SIGMUND S. GREENBAUM: I introduced the term sarcoidosis several years ago to denote the condition Kissmeyer carefully studied under the title of Boeck's disease, which may soon be accepted in America as a disease sui generis. There is confusion in nomenclature and perhaps in understanding of the conditions under discussion. If by Boeck's sarcoid is meant a purely cutaneous disease with multiple etiologic factors, one of which is tuberculosis, well and good. If, on the other hand, it is to be grouped as a cutaneous manifestation of sarcoidosis, then the diagnosis should be so qualified. I do not think that from the cutaneous phenomena alone it is always possible to make the latter diagnosis. When I saw this patient, I was under the impression that he presented one of the forms of tuberculous sarcoid, and I should not be at all surprised if tissue removed from him and injected into guinea pigs produced tuberculosis. In a case of this sort the simple designation sarcoid rather than sarcoid of Boeck would tend to clarify the situation.

Necrobiosis Lipoidica (Diabeticorum?). Presented by DR. JOHN B. LUDY.

C. W., a white woman aged 40, presents eight or ten various-sized areas on the lower parts of the legs. They began six years ago as reddish infiltrated spots on the anterior and lateral aspects of both legs and slowly increased by peripheral extension. The centers became yellowish, slightly scaly, shiny and stretched; the edges, brownish red and sharply marginated. There are practically no subjective symptoms. The patient is well nourished and has had no other illnesses of any

importance except an abscess around the apex of a tooth on July 2, 1934. The Wassermann and the Kahn test were negative; the basal metabolic rate was —2 per cent; repeated urinalysis showed no abnormality. The blood count on July 2, 1934, showed 83 per cent hemoglobin, 3,960,000 red blood cells and 8,000 white blood cells, with 58 per cent polymorphonuclear leukocytes, 40 per cent lymphocytes and 2 per cent eosinophils. On June 6, 1937, the sugar content was 92 mg. and the cholesterol content 210 mg. per hundred cubic centimeters. The sugar content on Sept. 21, 1937, was 89 mg. per hundred cubic centimeters. On May 7, 1938, a blood count showed 70 per cent hemoglobin, 4,570,000 red blood cells and 7,200 white blood cells, with 67 per cent polymorphonuclear leukocytes, 4 per cent monocytes, 1 per cent transitional forms and 26 per cent lymphocytes. The sugar content was 87 mg. per hundred cubic centimeters. The patient had received a gold preparation intravenously, without result.

DISCUSSION

DR. FRED D. WEIDMAN: Dermatologically, I think the eruption is necrobiosis lipoidica diabeticorum. Since this patient has not had diabetes, it might be designated as "necrobiosis lipoidica diabeticorum sine diabetes." A few cases have been described in which the dermatologic picture was like this one and without diabetes. Microscopically I was able to see a few giant cells in one corner of the section, but there was not sufficient tissue for further search.

DR. JOHN B. LUDY: This patient was presented two years ago for diagnosis (ARCH. DERMAT. & SYPH. **32**:825 [Nov.] 1935), and the majority of the members present expressed the belief that the condition was morphea—except Drs. Pillsbury and Greenbaum, who called it necrobiosis lipoidica diabeticorum.

DR. SIGMUND S. GREENBAUM: Have the lesions extended in the last two years?

DR. JOHN B. LUDY: They have, very much.

DR. HERMAN BEERMAN: I still think the condition clinically is morphea.

DR. EDWARD F. CORSON: In Detroit last January (ARCH. DERMAT. & SYPH. **38**:311 [Aug.] 1938) 2 cases were presented in the clinical session at the Harper Hospital, 1 that of a diabetic and the other that of a nondiabetic patient; the clinical pictures were indistinguishable.

DR. VAUGHN C. GARNER: My conception of morphea is of vascular dilatation at the periphery, forming a halo. I think the members were all struck with the fact that in these lesions the telangiectasia was central, which would support the diagnosis of necrobiosis lipoidica diabeticorum rather than morphea.

Lupus Erythematosus in Mother; Granuloma Annulare in Daughter. Presented by DR. EDWARD F. CORSON and DR. FRANK C. KNOWLES.

E. M. and J. M., a white woman and her child, aged 33 and 4 years, respectively, are presented. The mother has arrested lupus erythematosus, with atrophy of the skin of the nose. She was pregnant with the daughter while under treatment for the lupus erythematosus, which began seven years ago. She received fifty-seven intravenous injections of a gold preparation, the last on Sept. 10, 1935. The daughter shows a ringed eruption on the forearms, ankles and trunk, which began in April 1938. The left ankle shows the largest lesion and best exhibits the component papules at the rim. The central portion shows little or no atrophy. Roentgen therapy has been started on the daughter.

DISCUSSION

DR. CARROLL S. WRIGHT: The mother's appearance is a good example of what can be accomplished with gold therapy and of the extreme persistence that is sometimes necessary to bring about the desired result. This woman received

fifty-seven injections; sometimes the disease requires many more. There is no doubt of the diagnosis of granuloma annulare in the case of the child. The relationship is interesting but somewhat speculative.

DR. FRED D. WEIDMAN: From the cosmetic angle, I notice that there is an extremely salient margin to the depression of the mother's scar. I recall Dr. Fred Wise's stating that in this class of case the most satisfactory cosmetic result is obtained by simply cauterizing this salient margin with solid carbon dioxide. The more conspicuous the elevation around the scar, the more worth while it is to consider cosmetic treatment.

DR. EDWARD F. CORSON: The mother does not present an excellent cosmetic result, since she has a rather depressed scar. Nevertheless, she is satisfied with her appearance and does not desire further treatment. The interesting circumstance, of course, is the possibility of two paratuberculoid conditions in the same family.

Lineae Atrophicae. Presented by DR. JOHN B. LUDY.

D. B., a white girl aged 11 years, presents transverse markings on the outer surfaces of both thighs, most noticeable on the right side. They are erythematous or atrophic, the latter type being a few lines thick. The condition started eight months ago, four months after she had had an abscess in the right axilla. The present condition began on the right thigh and extended to the left thigh a few weeks later. At first it consisted of red macules, which became linear and later paled. The child was premature. She is now at her top weight—66 pounds (30 Kg.). There has been no sudden change in weight in the past.

DISCUSSION

DR. H. J. SMITH: Is it usual for the lines to be red first and then to become white?

DR. SIGMUND S. GREENBAUM: Since Ebert's work (ARCH. DERMAT. & SYPH. **28**:825 [Dec.] 1933) it is well known that stoutness or loss of a great deal of weight is not prerequisite to this condition, and I believe with him that these lesions represent some endocrine disturbance. The only finding I noted in this case which might point to such a disturbance is a tendency to excessive sweating.

DR. FRED D. WEIDMAN: This case illustrates the difference between striae distensae (hypertrophicae?) and striae atrophicae. Jadassohn mentioned the development of the latter transversely across the knee after attacks of typhoid fever, and the history here of an antecedent abscess is rather cogent. I take it that the abscess in the axilla did not lead to septicemia resulting in a condition of this sort, but there is a suggestive relationship.

Ichthyosis Hystrix. Presented by DR. JOHN B. LUDY.

W. W., a white boy aged 6 years, presents a universal eruption. It is scaly, with diamond-shaped or other polygonal figures of crackled skin. There is hystrix formation in places. It is associated with chronic ectropion. His face was swollen at birth. When he was 3 weeks old a miliaria-like eruption occurred on it. This was followed by dryness of the skin over the entire body. The patient is an only child. Except for occasional coryza, his health has always been good. He is undernourished (weight 47 pounds [21.3 Kg.]) and has diseased tonsils. His parents are well, but his mother has dry skin in winter. There is no other familial evidence of ichthyosis.

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading, Pa.: I was struck by the marked ectropion of the child. In the cases I have observed I do not recall seeing the lids pulled down as much as in this case.

DR. FRED D. WEIDMAN: I am wondering if Dr. Ludy has considered the diagnosis of erythroderma congenitale ichthyosiforme.

Dermatitis Vegetans. Presented by DR. ARTHUR GOMERSALL PRATT, Camden, N. J., and DR. FRANK C. KNOWLES.

E. D., a white woman aged 70, states that in May 1938 a small group of painless bullae developed on her back. In a few weeks the original lesions became crusted and granulomatous and had spread by peripheral extension downward. The spread was rapid at first, but after treatment by a private physician progress ceased. When she was first seen by us, on Aug. 9, 1938, a certain number of bullae were noted at the margin and in the central portion of the patch. The marginal bullae have continued to be a feature. The patch measures 15 by 9 inches (38 by 23 cm.). It is raised, sharply defined, crusted, oozing, pustular, gyrate and vegetating. No other areas of the skin are involved. The Wassermann and the Kahn test were negative. A blood count showed 70 per cent hemoglobin, 2,400,000 red blood cells and 8,800 white blood cells, with 52 per cent polymorphonuclear leukocytes, 36 per cent lymphocytes, 9 per cent eosinophils and 2 per cent monocytes.

DISCUSSION

DR. DONALD M. PILLSBURY: Has any search for blastomycetes been made?

DR. EDWARD F. CORSON: No.

DR. CARROLL S. WRIGHT: There are some other diagnoses that I believe could be considered here, such as pemphigus vegetans, which is likely, or mycosis fungoides of a localized type. I do not know whether a biopsy was performed in this case. I wonder if roentgen therapy would be of some value. The woman says she is much better.

DR. EDWARD F. CORSON: In his textbook, G. C. Andrews (Diseases of the Skin: A Text-Book for Practitioners and Students, ed. 2, Philadelphia, W. B. Saunders Company, 1938, p. 585) spoke of pemphigus vegetans and in parentheses added "dermatitis vegetans." He also placed dermatitis vegetans under another heading, as a separate disease. I am wondering if they are to be considered one and the same disease.

A Case for Diagnosis (Localized Pachyonychia Congenita?). Presented by DR. JOHN B. LUDY.

E. G., a white woman aged 22, as long as she can remember has had the following oral condition: The entire oral mucosa is the site of whitish desquamation. This varies in amount in the different regions affected, for as separation occurs the mucosa assumes a normal appearance Shortly thereafter the coating reappears, but only to flake off again in the course of time. The tonsils, the nasopharynx and the oropharynx are clear. The maternal grandmother and mother, a maternal aunt and 2 sisters have an identical condition. The patient is well nourished and considers herself healthy in all other respects. Many unsuccessful efforts have been made by the laboratories of three different hospitals, both by culture and by smear, to discover fungi. The flow of saliva is slightly slower than normal. Studies of the hydrogen ion concentration of the saliva with the Beckman p_H meter revealed the p_H of control saliva from a normal mouth to be 7.2, and of saliva collected from the patient (unstimulated), 7.3. The mouth was rinsed with approximately 3 cc. of sterile distilled water, and saliva collected after five-minute intervals gave a p_H of 7.3; 0.5 Gm. of sterile paraffin was chewed, and the stimulated saliva gave a p_H of 7.55. Scrapings from the buccal mucosa in the vestibule of the mouth were studied. Scrapings placed with a sterile loop needle in about 3 cc. of sterile distilled water gave a p_H of 7.4; scrapings placed in approximately 3 cc. of stimulated saliva gave a p_H of 8.04. The Wassermann and the Kahn test were negative.

DISCUSSION

DR. SIGMUND S. GREENBAUM: The only suggestion I can offer is that the condition is an atypical form of pachyonychia congenita in which the lesions are limited to the mouth. There is accompanying leukokeratosis in this condition. The fact that a similar condition is present in the 2 sisters, the grandmother, the

mother and a maternal aunt lends support to this diagnosis. Benson Cannon (ARCH. DERMAT. & SYPH. **31**:365 [March] 1935) has described a condition like this under the name "white sponge nevus of the mucosa."

DR. DONALD M. PILLSBURY: I questioned the girl closely as to whether the oral condition which was noted in her relatives was present at birth. She stated that it was. I do not believe it is possible to decide that it is localized pachyonychia congenita. Certainly the other symptoms of pachyonychia are lacking. I think it would be interesting to perform a biopsy, to see whether there is a nevoid change as such or possibly atresia of the glands of the mouth. I should like to suggest prescription of a high vitamin intake as an empiric measure.

DR. JOHN B. LUDY: In this family 3 girls, the mother and the mother's aunt have the same condition, but the brother and father do not have it. The 2 other girls have been seen by me. It seems to me that if Dr. Greenbaum's diagnosis were correct, some other members of the family should have some symptoms to corroborate it. It impresses me as some ichthyosiform condition which may be congenital. I propose to take the p_H of the saliva of the brother and the father, and I shall report the results later.

Multiple Glomus Tumors. Presented by DR. FRANCIS BETTERLY EVELAND, Wilkes-Barre, Pa.

M. S., a white woman aged 25, presents superficial pinhead-sized papules and slightly larger bluish red and smooth-surfaced ones on the left arm. The forearms show numerous pinhead-sized follicular hyperkeratotic lesions, some of which are excoriated. In addition, there are subcutaneous nodular lesions from 0.5 to 1 cm. in diameter in linear arrangement on the extensor surface of the left forearm, a hickory nut–sized tumor in the left axilla, a 0.5 cm. slightly tender nodule in the left palm, in the web of the thumb and finger, and a pea-sized bluish red nodule at the tip of the left index finger. All the lesions except that on the finger tip are painless. The condition is of eight months' duration. There are no subjective symptoms. The patient underwent subtotal thyroidectomy in March 1938. Urinalysis and a Wassermann test of the blood showed no abnormality. The tuberculin reaction (to old tuberculin intracutaneously) was negative. The histologic diagnosis was hemangioma or multiple glomus tumors.

DISCUSSION

DR. FRED D. WEIDMAN: This case parallels closely that which Dr. Fred Wise and I reported (ARCH. DERMAT. & SYPH. **35**:414 [March] 1937). In that case too the lesions were multiple, and pain, which is regarded as a sine qua non in the diagnosis of glomus tumor, was absent. In none of the lesions in the patient shown tonight was there pain—that is, the exquisite pain that characterizes this disease. She did volunteer, however, that the extremity of one finger was tender when pressed, which lends some support to the diagnosis of multiple glomus tumors. Histologically the picture is practically the same as that in Dr. Wise's case. If the diagnosis in the latter case was bona fide, the lesions in this one will certainly have to be considered glomus tumors. If not glomus tumors, the lesions must be classified as multiple hemangiomas. I must say that the consistently deep location of these lesions, their sharp circumscription and the type of stroma are altogether typical of multiple glomus tumors, but nerve tissue could not be demonstrated.

DR. SIGMUND S. GREENBAUM: I am willing to accept the histologic diagnosis of multiple glomus tumor, but I find it difficult to understand the enlarged lymph nodes in the left axilla, which suggest malignancy. I might add that I think the chest should be examined roentgenologically and one of the lesions in the axilla excised for histologic study.

DR. FRANCIS BETTERLY EVELAND, Wilkes-Barre, Pa.: Another lesion, that in the web of the hand, was tender. Lymphoblastoma was considered.

A Case for Diagnosis (Vitiligo? Aberrant Lupus Erythematosus?). Presented by DR. JOHN B. LUDY.

In H. S., a white boy aged 6 years, a red eruption developed six months ago and was followed by scaling. The color gradually faded and left a sharply marginated pigmented area on the forehead and upper part of the face. The child has never been ill, his appetite is good and his diet is well balanced. His tongue is coated; the papillae are clear at the edges and the tip. There is some definite mottling on the forearms. A blood count showed 77 per cent hemoglobin, 4,200,000 red blood cells and 5,400 white blood cells, with 52 per cent polymorphonuclear leukocytes, 40 per cent lymphocytes and 7 per cent monocytes.

DISCUSSION

DR. FRED D. WEIDMAN: I offer the diagnosis of berlock dermatitis. The parents told me that the boy's hair was smeared with rose oil for a long while immediately before the appearance of the dermatitis.

DR. EDWARD F. CORSON: I did not get that history.

DR. DONALD M. PILLSBURY: As I understand it, the condition is at an end stage now, with the remains of an inflammatory eruption. I could not see any evidence of lupus erythematosus. The patient was particularly interesting to me, because in following a number of Negro children at the Children's Hospital I have been struck by the varying pigmentary responses following various dermatoses, such as pityriasis rosea in some cases, depigmentation in others and sometimes hyperpigmentation in one area and depigmentation in another in the same case. I do not see how the dermatitis can be attributed to the application of an ointment to the scalp, because the scalp was not involved. The picture is not that of vitiligo.

DR. SIGMUND S. GREENBAUM: I agree with Dr. Pillsbury.

Rosacea-Like Tuberculid of Lewandowsky. Presented by DR. THOMAS BUTTERWORTH, Reading, Pa.

J. K., a white woman aged 36, presents a bright erythema over both malar regions. Under diascopic pressure numerous pinhead-sized yellowish brown puncta are seen. The condition began five years ago as a rosacea-like erythema over the left malar region. In a few months a similar erythema occurred over the right cheek bone. The patient had frequent night sweats, particularly at the time of the menses. Both the grandmother and a paternal aunt died of pulmonary tuberculosis. The patient frequently visited and lived periodically each year with her aunt prior to the latter's death. The patient had pleurisy in 1918 and 1931; she has frequent colds and laryngitis and had influenza and pneumonia in 1918. Physical, fluoroscopic and roentgen examination of the chest revealed bilateral infiltrative tuberculosis. Apparently the patient has had a recent flare-up superimposed on an older chronic lesion. The Kahn and the Kolmer-Wassermann test were negative. Urinalysis and a blood count gave results within normal limits. The tuberculin test has not yet been done. The patient has received a total of 790 mg. of sodium gold thiosulfate over a period of five months, with slight improvement.

DISCUSSION

DR. SIGMUND S. GREENBAUM: I agree with the diagnosis.

DR. ABRAM STRAUSS: I think the condition is rather typical.

DR. FRANK C. KNOWLES: Clinically, I do not think it resembles Lewandowsky's tuberculid. The lesions are not elevated; they are small and rather hemorrhagic, and the patient says that they have never been raised above the surface of the surrounding skin. The distribution is rather typical of the diagnosis, but I think the diagnosis cannot be proved without a biopsy.

DR. VAUGHN C. GARNER: The distribution is rather atypical, since the lesions are lateral to the malar regions. I was struck by the absence of the typical

miliary yellowish puncta which one sees in this type of tuberculid. An alternative diagnosis might be telangiectatic lupus erythematosus.

Dr. THOMAS BUTTERWORTH, Reading, Pa.: There seems to be a great misunderstanding about just what is meant by Lewandowsky's tuberculid. Some dermatologists seem to think it should be included in lupus miliaris disseminatus faciei.

DR. FRED D. WEIDMAN: I understood from the history that I obtained from the patient that the first phenomenon was a swelling of the cheeks, which became tumid and red. Were these nodules associated at that time or not? Did Dr. Butterworth ever see her when her cheeks were tumid and red? I considered a diagnosis of erythromelalgia from the history.

DR. THOMAS BUTTERWORTH, Reading, Pa.: I have never been able to discern the brownish nodule without diascopic pressure.

Acanthosis Nigricans Juvenilis. Presented by DR. THOMAS BUTTERWORTH, Reading, Pa.

M. E. K., a white girl aged 16, exhibits numerous closely set dark brown and black warty excrescences forming a collar and large pigmented patches in the axillas, beneath the breasts, in the cubital spaces, in the small of the back and in one popliteal space. The normal lines of the skin are exaggerated. The distribution of hair is indicative of pituitary disturbance, although it is not of the true male type. The patient is a rotund healthy girl weighing 231 pounds (104.8 Kg.). The thyroid is not palpable. Except for great obesity, physical examination showed no essential abnormality; the obesity is considered to be of the pituitary type. The eruption began as a progressive discoloration of the involved areas two or three years ago. The blood count and the bleeding and coagulation time were within normal limits. Urinalysis showed no abnormalities, and the Kolmer and the Kahn test were negative. The basal metabolic rate was +4 and +9 per cent in two determinations. Roentgenograms of the sella turcica were normal. The report of the biopsy follows: "The entire surface of the skin is verrucous. There is hyperkeratosis over the entire surface, but not the slightest mixture of parakeratosis. The stratum granulosum is thin but definite and the prickle cell layer slightly thickened. There is a barely recognizable excess of pigment in the basal layer. The papillae are long and narrow as they extend into the acuminate projections of the surface." The patient lost 12 pounds (5.4 Kg.) in five weeks on a restricted diet and 2 grains (0.13 Gm.) of thyroid three times a day. There has been no gross change in the cutaneous picture.

DISCUSSION

DR. FRANK C. KNOWLES: I recall a case diagnosed as one of juvenile acanthosis nigricans in which bullae suggesting epidermolysis bullosa developed on the forearms. In that instance there were two conditions: a curious pigmentary change in the area affected by acanthosis nigricans and the bullous lesions, which had developed since infancy. A combination such as that is rather interesting in connection with the present condition. I think it might be worth while in the present case to go into the question of whether slight traumatism gives rise to cutaneous lesions.

DR. JOHN B. LUDY: My patient with acanthosis nigricans was 5 or 6 years of age when I first saw her, and she is now a woman of 25, with 2 children. She had tuberculous peritonitis and was operated on. The operation had no effect on the progress of the acanthosis nigricans.

A Case for Diagnosis (Idiopathic Keloid?). Presented by DR. DONALD M. PILLSBURY.

C. T., a white woman aged 35, presents a nodular dermatosis distributed on the extremities, principally on the extensor surfaces. The lesions appear as small

painless erythematous nodules. Spontaneous involution occurs over a period of several months, and a depressed, sharply punched-out scar remains. The dermatosis is of ten years' duration, and approximately thirty lesions have appeared. The patient's general health has been good throughout the course of the dermatosis. The general physical examination reveals no findings of note. The patient uses iodized salt. The Wassermann and the Kahn test were negative. The blood count was normal. The changes seen histologically were typical of keloid. Two of the lesions have been treated with a single massive dose of roentgen rays, without effect.

DISCUSSION

DR. ABRAM STRAUSS: I saw this woman fifteen years ago, with about three lesions on the right leg near the knee. I made a diagnosis at that time of idiopathic keloid and predicted that in years to come she would get other lesions on the legs and arms. This has since occurred.

DR. FRED D. WEIDMAN: The sections showed the histologic structure of keloid. The patient has shown me a number of scars, including that from vaccination, and in none of them has keloid developed. This case is evidently one of generalized keloidal diathesis. I asked about mosquito bites, and she said she did not recall having any nodules after mosquito bites.

DR. SIGMUND S. GREENBAUM: I think this condition is well known and described in most textbooks under the name fibroma durum (subepidermal nodular fibrosis), and I have observed 2 or 3 other instances in the past eighteen months. The lesions begin spontaneously, enlarge to a certain size and then in a variable period of time tend to undergo regression, leaving pigmentary atrophic spots. I saw a patient last week who had half a dozen lesions. They are usually on the lower extremities.

DR. FRED D. WEIDMAN: Fibroma durum is usually of various sizes. Where the lesions are of such a uniform size, they should be rated more as keloids than as fibroma durum.

DR. DONALD M. PILLSBURY: These lesions rise and go through their evolution slowly and end with a depressed scar with slight pigmentation. I do not believe that these lesions are fibroma durum, because of the marked erythema associated with them and because of their spontaneous involution.

Lupus Vulgaris Erythematodes (Leloir). Presented by DR. JOHN B. LUDY.

THOMAS BUTTERWORTH, M.D., *Chairman*

Oct. 21, 1938

HERMAN BEERMAN, M.D., *Secretary*

A Case for Diagnosis (Linear Nevus? Linear Neurodermatitis?). Presented by DR. DONALD M. PILLSBURY.

S. L., a white woman aged 28, presents two somewhat indurated linear excoriated plaques approximately 4 cm. in length on the under surface of the right side of the chin. The upper lesion is about 5 mm. in width and the lower approximately 3 mm. The appearance of the lesions varies with the amount of the excoriation. Occasional follicular pustules are seen. The condition began about eleven years ago, and the extent of the area involved has changed little. The Wassermann reaction of the blood was negative. The patient has been treated by ultraviolet and roentgen irradiation and various local applications. Roentgen therapy was effective at first, but the pruritus has now returned.

DISCUSSION

DR. W. O. ROOP, Atlantic City, N. J.: This patient does not have linear nevus, as the lesions are pruritic. I agree with the diagnosis of neurodermatitis and suggest lichen planus as an alternative diagnosis.

DR. H. J. SMITH: This patient has linear nevus.

DR. EDWARD F. CORSON: This patient has linear nevus. Nevi may begin some time after birth. Linear nevus is usually unilateral; lichen planus is usually bilateral.

DR. REUBEN FRIEDMAN: I suggest that the eruption may be a factitious dermatitis.

Acute Infectious Eczematoid Dermatitis Responding to Sulfanilamide.
Presented by DR. CARROLL S. WRIGHT and DR. REUBEN FRIEDMAN.

I. M., a white man aged 39, states that three weeks ago the skin about the sinal orifice from an old osteomyelitic infection became red and painful, the condition spreading peripherally. Two days ago the skin of the upper two fifths of the extensor surface of the left forearm presented an acute dermatitis, the center of which was the discharging sinal orifice. The patient complained of marked pain, intense itching and insomnia. The clinical picture today differs from that of two days ago in that there is no pain and no itching, the involved area has become dry, scaly and considerably paler, and the moisture at the sinal orifice is scanty. On aerobic blood agar many colonies of Staphylococcus aureus haemolyticus (pure culture) developed; anaerobically many colonies of Streptococcus haemolyticus (pure culture) developed. Fifteen grains (0.97 Gm.) of sulfanilamide was administered every four hours, starting two days before presentation, with the aforementioned improvement. No local treatment was given.

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading, Pa.: I have had no experience with sulfanilamide in cases of this type, but for dermatitis herpetiformis sulfanilamide has produced the most satisfactory results I have seen.

DR. EDWARD F. CORSON: At the Jefferson Hospital 3 ward patients are being treated with sulfanilamide. One patient has an ulceration on the arm, one an ulcer on the leg and the third an ulcer on the side of the head. Results have not been encouraging so far, though cultures indicate that the remedy is appropriate.

NOTE.—Within one week from the time sulfanilamide therapy was instituted in this case the lesion was completely healed.

Chronic Streptococcic Ulcer of the Skin Responding to Sulfanilamide.
Presented by DR. CARROLL S. WRIGHT and DR. REUBEN FRIEDMAN.

J. V., a white man aged 82, about eight years ago scratched a "pimple" on the anterior aspect of the left leg until it became raw and bleeding. A progressive ulceration developed which, despite all therapy, has not healed. Two days ago there was on the anterior aspect of the middle of the left leg a roughly oval sharply marginated ulcer measuring about 11 by 5.5 cm. Near the upper posterior border there was, two days ago, well marked undermining of the edges. Pressure on the edge resulted in the exudation of serous yellow-brown fluid. The floor of the ulcer was covered with heaped-up irregular masses of smooth shining granulation tissue bathed in thin serous exudate. It also showed two small patches of yellow-green necrotic tissue. Encircling the lesion was a band of violaceous red shiny thickened skin about 4 to 5 cm. in width. It was tender in places. With a few changes to be noted, the clinical picture is the same today. Serologic tests of the blood repeatedly gave negative results. Aerobic cultures on blood agar were overgrown with contaminated Bacillus subtilis. Anaerobically a pure culture of Str. haemolyticus was secured. The patient was given 15 grains (0.97 Gm.) of sulfanilamide every four hours, beginning two days ago. This treatment has

produced a distinct improvement. The lesion looks and is drier; the granulation tissue seems healthier, and the undermined edges have disappeared. The tissues about the ulcer are paler and are not tender.

DISCUSSION

DR. CARROLL S. WRIGHT: This patient was in the hospital for complete rest for a while. He was thoroughly studied by many departments, including those of medicine and surgery, and the surgeons refused to attempt skin grafting because they feared it would not "take." Although the diagnosis of syphilis was questionable, the patient was given antisyphilitic therapy, without improvement. The first benefit we have seen in this case has been in the last two days, under sulfanilamide therapy.

DR. SIGMUND S. GREENBAUM: The edges of such ulcers make one think erroneously of syphilis. I consider them a superficial form of pyoderma gangraenosum. I believe the cases recently reported by M. H. Goodman (*J. A. M. A.* **111**:1427 [Oct. 15] 1938) are of the same type. I have been able to prove experimentally that a symbiotic infection is necessary to produce some ulcers of this type. When either type of living organism recovered from such ulcers was injected intraepidermally, nothing developed; when both types were injected together, a definite ulcer similar to the undermining type of pyoderma gangraenosum developed. It is an important finding that sulfanilamide has a beneficial effect on such ulcers.

DR. REUBEN FRIEDMAN: In H. W. Barber's article several years ago (Prognosis in Streptococcal Infections of the Skin, *Lancet* **2**:35 [July 6] 1935), he stated that "streptococcal lesions always become secondarily infected with staphylococci." In Goodman's recently reported cases of chronic streptococcic ulcer of the skin, however, evidently no symbiotic infection existed, for he was able to recover a beta hemolytic streptococcus in pure culture in all 3 instances. Moreover, he saw a similar ulcerative lesion produced on the skin of 1 of his patients after the accidental transfer of the organism. Indeed, it was the realization of the fact that he was dealing with a purely streptococcic infection that led him to try sulfanilamide therapy. Because we recovered a pure culture of beta hemolytic streptococcus in our patient's chronic ulcerative process, we resorted to sulfanilamide therapy, with the present encouraging result.

Phenolphthalein Eruption (Extensive Hyperpigmentation). Presented by DR. HERMAN BEERMAN.

J. B., a Negress aged 39, for the past three summers has had a recurrent scaly eruption of generalized distribution which, on improving, has left a bizarre pattern of hyperpigmentation at the sites of previous efflorescence. The present attack began this summer, and the patient was left with the present hyperpigmentation. The eruption is associated with generalized pruritus. She takes various medicaments, including senna, magnesium sulfate and a proprietary phenolphthalein preparation. She noted a definite relation between the recent acute flare-up and the taking of the proprietary preparation. The patient is a healthy Negress with extensive areas of hyperpigmentation involving most of the trunk and the extremities and, to a lesser degree, the face. There is questionable pigmentation in the mouth. In certain areas the hyperpigmentation is spotted. The normal skin stands out in relief as light brown islands. The Wassermann and the Kahn reaction of the blood were negative. Scrapings showed no fungi. The patient was given an antipruritic lotion.

DISCUSSION

DR. J. P. GUEQUIERRE: I agree with the diagnosis and think this eruption the most spectacular one due to phenolphthalein I have ever seen.

DR. H. J. SMITH: I saw a few days ago an eruption just as extensive as this in a patient who also had bullae. My patient had the eruption three times at intervals of about six months. All of the bullae, some as large as a hand, were flat and flaccid. They always occurred on the same sites.

DR. SIGMUND S. GREENBAUM: The eruption mentioned by Dr. Smith looked much like a phenolphthalein eruption, but the history showed that the patient had been taking a coal tar product and iodides. It is not my impression that coal tar products will produce a bullous eruption in conjunction with the erythematous pigmented eruption that comes with intolerance to those drugs. The iodides occasionally produce a bullous eruption. It is believed by some physicians that epinephrine is the antidote for the bullous iodide eruptions, but I have had no personal experience with it.

DR. H. J. SMITH: I was told that my patient had been taking phenolphthalein.

DR. HERMAN BEERMAN: I should give this woman more phenolphthalein if I were not afraid of a violent reaction.

DR. ALLEN D. KING, Wilmington, Del.: I think a word of commendation should be said for the diagnostic persistence of the presenter. The patient had repeatedly denied taking laxatives or other preparations containing phenolphthalein until she was asked to bring in all the medicines she had, and thus the proprietary preparation came to light.

Pemphigus. Presented by DR. CARROLL S. WRIGHT.

M. F., a white man aged 53, states that four months ago he noticed crusted lesions on the scalp, accompanied with loss of hair. Lesions soon appeared on the face and sternum and have now spread over the trunk and extremities. On the scalp, face and trunk there are a number of crusted lesions of varying size. The forearms show crusting and bleb formation. The Wassermann reaction of the blood was positive. The blood count showed 4,480,000 red blood cells, 13,800 white blood cells and 75 per cent hemoglobin. The patient was given a high vitamin diet and 300,000 units daily of vitamin D (viosterol), and colonic irrigations were done, all without benefit.

DISCUSSION

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I agree with the diagnosis. Some years ago I had 2 patients with pemphigus in one family. The first patient was a physician. Some years after his death his brother came to my office with a pustular eruption on the scalp. He said "I have pemphigus." His disease had a short course with death about six months later. I think this is the only record of 2 cases of pemphigus in one family.

DR. THOMAS BUTTERWORTH, Reading, Pa.: This case might be a good one in which to try sulfanilamide.

DR. PATRICIA DRANT: Dr. Ludy and I have had success with vitamin D therapy in cases of pemphigus. This man's condition should respond to this treatment, particularly since he has had no lesions of the mucous membrane. Occasionally, in cases in which it has been difficult to secure improvement, I have had success with frequent small (50 cc.) daily blood transfusions. When there are many bullae, intravenous dextrose speeds up regression. Then viosterol four days a week and arsenic trioxide and quinine three days a week are beneficial.

DR. D. M. SIDLICK: I have treated pemphigus in 3 cases with germanin. One patient has been discharged from a hospital for the past twenty-one months and 1 for fourteen months, and 1 is still under treatment. I do not wish to maintain that germanin is specific for pemphigus, but it seems to have produced a cure in 2 of my cases. The first patient received about 14 Gm. in eleven weeks, and the second patient has received 12 Gm. The third patient has received only two injections, and her lesions have improved. I think germanin is worth a trial.

DR. SIGMUND S. GREENBAUM: The cases of the brothers Dr. Schildkraut mentioned were reported in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**33**:730 [April] 1936) by Dr. Samuel Feldman. They were, I believe, the first cases of pemphigus reported in near relatives. Two or three years ago I attended a woman with pemphigus. Her sister had died of the disease five years earlier while under my care. The second sister died suddenly while she was taking large doses of

vitamins A and D. This is the first report of pemphigus in sisters. About seventeen years ago I saw a dentist with pemphigus, who died; four or five years later his wife had benign pemphigus, from which she recovered. The present patient displays unusual pemphigus vulgaris, because the blebs are flaccid and the eruption does not look like the usual severe type of pemphigus vulgaris. It may be the Senear-Usher type of pemphigus vulgaris. It may well be that some of the therapeutic agents advised here will lead to recovery in this particular patient. I have used transfusions and have administered germanin, sulfanilamide, large doses of vitamins A and D, tryparsamide and many other substances, but most of the patients have died. Occasionally a patient gets well, but it is difficult to say that any particular drug has produced the result. It is known that coagulen and iron cacodylate have given good results, but, as with the other reported remedies, when some one else tried them they did not seem to be effective.

DR. THOMAS BUTTERWORTH, Reading, Pa.: About two years ago I presented a case of pemphigus foliaceus which had responded favorably to vigorous therapy with all types of vitamins and activated charcoal, recommended by Dr. Greenbaum.

DR. SIGMUND S. GREENBAUM: In patients with pemphigus of two or three months' duration, with a number of blebs and a little fever, certain vaccines cause a slight elevation of temperature and cough. The patient seems to go downhill after the second, third or fourth dose. In some instances, when the nonspecific therapy is stopped, improvement above the patient's previous best is noted. Activated charcoal administered intravenously acts similarly. It is a purely nonspecific agent, acting through the reticuloendothelial system, which takes up foreign particles and presumably increases the resistance of the patient.

Epidermolysis Bullosa Hereditaria. Presented by DR. HENRY H. PERLMAN.

This case, presented for follow-up and therapeutic suggestions, was reported previously by Drs. E. F. Corson and H. Harris Perlman (*M. J. & Rec.* **136**:67 [July 20] 1932).

DISCUSSION

DR. EDWARD F. CORSON: I have not seen the patient for about six years, but when I saw her the eruption was much more typical of epidermolysis bullosa than it is now. I might mention especially the good condition of the girl's finger nails. I am surprised, after this lapse of time, that she shows such perfect nails, because ordinarily in this disease one finds an atrophic or dystrophic scarred appearance of the nails and nail beds.

CLEVELAND DERMATOLOGICAL SOCIETY

JOHN A. GAMMEL, M.D., *President*

Sept. 22, 1938

CHARLES G. LAROCCO, M.D., *Secretary*

JAMES R. DRIVER, M.D., *Reporter*

Lupus Erythematosus (Senear-Usher Syndrome). Presented by DR. W. F. SCHWARTZ (from the Department of Dermatology and Syphilology, Cleveland City Hospital).

L. B., a Negress aged 51, was in good health until three months ago, when she noticed an eruption about the umbilicus, the forehead, the temples, the right forearm and the left thigh.

The lesions consist of grouped vesicles, some almost pea sized and others smaller. In some areas the lesions have involuted, leaving scaly, depigmented and

moderately atrophic spots. In the temporal area the involvement extends beyond the hair border, producing areas of alopecia about 1 inch (2.5 cm.) in diameter. These lesions are characteristic of lupus erythematosus. There are no lesions on the mucous membranes. There is some pruritus. Nikolsky's sign was not elicited.

Roentgenograms of the chest were essentially normal. There were 4,500,000 erythrocytes and 12,900 leukocytes. The differential leukocyte count was normal.

A biopsy specimen taken from the temporal lesion included hairs and sebaceous glands. The epidermis was thickened. There was patchy hyperkeratosis about the follicular openings, together with decided parakeratosis and hypergranulosis in the same regions. Except along one margin, where it was normal, the epithelium was the seat of moderate hyperplasia. The pegs were elongated and broadened. The basal layer was slightly frayed, and the cells had lost their pigment. There were mild intercellular edema and formation of a few vesicles between the corium and the epidermis. A few red blood cells and polymorphonuclear leukocytes were present in these vesicles, and many of the latter cells infiltrated the corium immediately surrounding them. There was mild edema of both the superficial and the deep portion of the corium, and the collagen bundles were broad and pale staining. Especially in the papillary and subpapillary layers of the corium there were numerous focal collections of lymphocytes and plasma cells together with a few large cells. These were frequently perivascular, but in some places they were not related to the blood vessels. A few lymphocytes and plasma cells were distributed diffusely throughout the superficial portion of the corium.

DISCUSSION

DR. E. W. NETHERTON: There is a lesion back of the right ear that shows definite follicular plugging. I think this is lupus erythematosus, but I do not feel at present that I could make a diagnosis of the Senear-Usher type of the disease. The patient has no definite bullous lesions at present.

DR. J. R. DRIVER: In all the cases of Senear-Usher disease that I have observed there have been lesions involving the borders of the scalp. The umbilicus also is commonly involved. This distribution, I feel, is characteristic.

DR. H. N. COLE: The symmetry of the eruption, with lesions that look like lupus erythematosus and pemphigus, is in favor of the diagnosis as presented.

Secondary Syphilis (Relapse or Reinfection?). Presented by DR. GERARD ANTHONY DEOREO (from the Department of Dermatology and Syphilology, Cleveland City Hospital).

H. N., a Negress aged 28, was seen in the outpatient department of the Lakeside Hospital in October 1929, because of a sore on the vulva. Dark field examination was not performed, but the Wassermann reaction of the blood was strongly positive. A diagnosis of seropositive primary syphilis was made. After five intravenous injections of arsphenamine the lesions healed, and she failed to return for further treatment.

She returned in April 1932 for treatment of acne. At this time the Wassermann reaction of the blood was negative. Antisyphilitic therapy was resumed, but after the second injection of a bismuth compound the patient failed to return for treatment

On June 20, 1938, she was seen in the gynecologic clinic of the outpatient department, complaining of menorrhagia. At this time the Kline diagnostic and exclusion tests of the blood gave negative results.

On September 15 she returned to the dermatologic clinic, complaining of a generalized eruption of three weeks' duration. The eruption is maculopapular and coppery red. There are lesions on the trunk and scattered sparsely on the extremities and on the palms and soles. There are no lesions in the mouth or on the genitalia or the uterine cervix.

There has been frequent sexual intercourse. In one instance, about three months ago, intercourse was with a man known to have early infectious syphilis.

The Wassermann and Kline reactions of the blood were strongly positive. Examination of the spinal fluid gave normal results.

Histologic examination of a cutaneous lesion showed a thick layer of keratin. There was no hypergranulosis or parakeratosis. The pegs were elongated and fairly regular, as were the papillae, which were separated from the epithelium by a layer only three to five cells thick. There was a dense, sharply circumscribed cellular infiltrate in the superficial portion of the corium. This was composed of lymphocytes, plasma cells and a few mononuclear cells. The infiltrated part of the corium was slightly edematous. Blood vessels deep in the corium showed no significant change.

DISCUSSION

DR. G. W. BINKLEY: I believe there is just as much evidence in favor of reinfection after a biologic cure as there is for a relapse. Arsenical therapy had been given, and subsequent blood tests gave negative results as late as June 1938, or nine years after this treatment. Unfortunately, there is no evidence of a primary lesion and the patient was not seen early enough for the development of positive serologic changes to be watched. Rigid criteria for the diagnosis of reinfection are lacking, but its probability is most suggestive. Finally, the most important evidence against a relapse is that of a generalized maculopapular symmetric eruption not characteristic of the localized eruption that one would expect to see in syphilis after this long interval.

DR. H. N. COLE: If there is anything in Brucgaard's report that 30 per cent of syphilitic persons are normal on physical examination, I suppose one must accept the fact that certain persons are cured with a small amount of treatment. It was difficult to accept this patient's eruption as a relapse. In syphilis that relapses after nine years, one would expect a localized rather than a generalized eruption. This is particularly unlike a relapse because there are lesions on the palms and soles. I grant that with an early relapse—in a matter of a year or so—there may be a generalized eruption, but this is nine years afterward, and it would be most unusual. Even though no new primary lesion can be seen, and the serologic changes cannot be brought out, I am willing to accept this condition as a probable reinfection.

DR. JOHN A. GAMMEL: I believe the consensus is that it is a reinfection.

DR. R. E. BARNEY: I think the question of plasma cells should enter here. If there were more plasma cells, the diagnosis would be more in favor of syphilis than lichen planus, of which I heard some suggestion.

DR. W. F. SCHWARTZ: In early syphilis the plasma cells are more numerous than in late syphilis. I think that is evidence in favor of a reinfection rather than a relapse in this case.

DR. JOHN WORK (by invitation): Pathologists recognize the fact that with many slides the best one can do is make a diagnosis of chronic or acute inflammation. The round cell infiltration present in the upper part of the corium in this section suggests to me a diagnosis of lichen planus rather than syphilis.

DR. E. W. NETHERTON: The infiltration of round cells in this section is not definitely bandlike, as in lichen planus. I should hesitate to make a diagnosis of lichen planus from this slide.

Epidermolysis Bullosa Acquisita. Presented by DR. E. W. NETHERTON and DR. GEORGE HASKEL CURTIS (by invitation).

G. F. C., a man aged 52, has always been in good health. There is no history of pemphigus or other bullous diseases. He states that he knows of no similar disease among his blood relatives.

The first bullae were noticed in December 1937, on the thumbs (after using a wrench) and on the tongue. Since then these bullae have occurred on the palms and palmar surfaces of the fingers, on the elbows, the knees, the toes and the buccal mucosa along the line of occlusion. The blisters have varied from the

size of a pea to that of a half dollar, tensely filled with either hemorrhagic or clear fluid. The patient has always associated their appearance with manual labor or trauma. On healing, the blisters rupture or dry and desquamate. The new skin was never pigmented. There is no history of arsenical medication. The patient has been concerned because the disease has prevented him from working.

The following types of cutaneous lesions were present when the patient was first seen: (1) many small hyperkeratotic and wartlike papules on the palms; (2) a large ruptured bullous lesion with a slightly erythematous base, on the right knee; (3) tense, pea-sized hemorrhagic bullae on the palms and fingers; (4) scars, atrophy and scaling of the skin over the elbows; (5) two pea-sized, tense, hemorrhagic bullae on the left buccal mucosa along the line of occlusion. None of the lesions were tender. With moderately severe pinching bullae were produced on the elbows. At present there are several hemorrhagic bullae on the fingers and ruptured bullae on the knees.

The hemogram was normal; the platelet count was 280,000; the clotting time eight minutes, and the bleeding time, one and one-half minutes. The clot retraction was normal, as was the urine. The Wassermann and Kahn reactions of the blood were negative.

Tissue for biopsy was taken from the edge of a bulla on the palm in the groove between the thenar and hypothenar eminences. At one end of the section there was coagulated fluid containing red blood cells and leukocytes, dividing the epidermis in the prickle cell layer. In some places the division severed the papillae so that only the rete pegs could be seen in the uppor portion of the corium. Spongiosis could be seen in the lower layers of the epidermis in the region of the bullous formation, together with invasion by a few round cells. The papillae beneath the bulla showed edema, dilatation of blood vessels and round cell infiltration, which was mostly perivascular. The edema, in diminishing amount, extended down to the subcutaneous tissues, as did the perivascular infiltration.

In the middle of the section there was decided edema of the papillae, with complete separation of the tissues from the basal cell layer. The edema in the corium, extending to the subcutaneous tissue, separated the connective tissue so that pools were formed in which islands of blood vessels were seen in a few places. Extravasation of red blood cells in the upper part of the corium was in this area.

Epidermolysis Bullosa Complicated by Pulmonary Tuberculosis. Presented by DR. FRANK MCDONALD (from the Department of Dermatology and Syphilology, Lakeside Hospital).

M. P., a poorly nourished man aged 33, of Spanish descent, recalls having had clear or hemorrhagic bullous eruptions over most of his body, especially on the legs, feet, hands, elbows, shoulders, back and abdomen, since the age of 4 years. He has never been completely free of lesions, the disease varying in intensity. The bullae tend to break, leaving raw, exuding surfaces which either heal with scar formation or subside spontaneously, leaving slightly pigmented areas. The present exacerbation began two months ago on the legs and forearms. Scarring and atrophy of the skin have caused loss of function of the hands; otherwise the patient has no discomfort.

On the anterior aspects of both legs from the patellas to the ankles there is a diffuse red atrophic dermatosis with some scaling, some exudation and several bullae. There are similar lesions over the wrists. Both elbows are covered with diffuse redness and scaling. The hands show atrophy, scarring and contractions of the skin, with deformity of the fingers and absence of the nails. The feet show atrophy and scarring of the skin and loss of the nails. Over the lower part of the vertebral column are four bullae and a few areas of pigmentation. Except in the affected areas the skin appears normal. There are no lesions of the mucous membranes.

Roentgenograms of the chest revealed apical tuberculosis; the sputum contained tubercle bacilli. The Wassermann and Kline reactions of the blood were negative.

The protein content of the plasma and the calcium, phosphorus, chloride and non-protein nitrogen contents of the blood were normal. The ascorbic acid content of the serum is 0.24 mg. per hundred cubic centimeters. Roentgenograms of the hands and feet showed no involvement of bone.

A specimen of apparently normal skin showed a slight degree of keratosis of the epithelium, no bullae and no acanthosis. The connective tissue showed slight edema but no cellular infiltrate. Stains for elastic tissue showed slight diminution in its amount.

A specimen from a lesion of the leg showed the same characteristics as the aforementioned specimen, plus a moderate degree of lymphocytic infiltrate in all layers, with a moderate degree of irregular edema.

DISCUSSION

DR. H. N. COLE: The patient presented by Dr. McDonald has had his disease so long that in some ways he does not show the picture that one would ordinarily expect. He does not have milia, which are ordinarily seen on the backs of the digits and on the elbows and knees. The process is in the atrophic stage. In fact, he has had so many different attacks that it has finally resulted in complete absence of the nails.

I wonder if one should not classify the disease of Drs. Netherton and Curtis' patient, coming on so late in life, under the name acquired epidermolysis bullosa. If followed, I wonder if some other condition can be found to explain it. For example, is there any history of ingestion of drugs? I am not familiar with any case of so-called acquired disease coming on so late in life.

DR. E. W. NETHERTON: I cannot give any information as to how late it may occur, but when I first saw the patient I was confused as to whether this was erythema multiforme or epidermolysis bullosa. There are certain definite characteristics. There is definite atrophy on the elbows and knees, which resulted from previous lesions. None of the lesions observed by my associates and me have been associated with erythema. They come up suddenly and always after the slightest trauma. When the patient does not work they clear up, but if he returns to work he has numerous lesions on the hands. Mowing the lawn will bring these lesions on. He had one today on one of the fingers, produced by opening the car door. When these things are considered—the absence of erythema and the usual things seen in erythema multiforme, and the fact that they follow immediately after trauma—it seems that that disease is the more likely. I do not believe there is any history of drug ingestion, except that on the basis of erythema multiforme he was given some salicylates for a week or ten days, without any improvement. If the slightest trauma is involved, these hemorrhagic, bluish lesions develop.

Acute Meningovascular Syphilitic Neurorelapse. Presented by DR. FRANK MCDONALD (from the Department of Dermatology and Syphilology, Lakeside Hospital).

D. P., a man aged 23, was first seen in the outpatient department of Lakeside Hospital in January 1936, complaining of pain up and down the spine for six weeks. The Wassermann reaction of the blood was strongly positive with all antigens. The spinal fluid showed 60 mononuclear cells; the Pandy reaction was 1 plus, the mastic curve 2210000000, and the Wassermann reaction negative with 0.1 cc., 3 plus with 0.5 cc. and 4 plus with 1 cc. of antigen. There was no history of primary or secondary syphilis. The symptoms were relieved by administration of thiobismol and potassium iodide. A diagnosis of early meningovascular syphilis was made. Between March 1936 and July 14, 1938, the patient received fifty injections of mapharsen and fifty intramuscular injections of a bismuth preparation in alternating courses. The spinal fluid in February 1937 showed 8 cells per cubic millimeter. The Pandy reaction was negative, the mastic curve normal and the Wassermann reaction negative with all antigens. In May 1938 the patient com-

plained of occipital headaches. On July 28, while caddying on a golf course, he was struck in the right parietal region by a golf ball but did not lose consciousness. After lunch a week later he felt drowsy and shortly thereafter was found unconscious and in convulsions.

The temperature was 37.6 C. (99.7 F.), the pulse rate 120, the respiratory rate 24 and the blood pressure 130 systolic and 65 diastolic. He was in coma and under the influence of paraldehyde. The pupils were equal and did not respond to light. The eyes deviated to the left, and there was quick nystagmus to the left. The optic disks showed nasal blurring bilaterally. The achilles and patellar reflexes were sluggish, and the abdominal reflexes were absent. The Kernig and Babinski signs were absent.

The urine was normal. Examination of the blood showed 22,800 leukocytes, with 93 per cent polymorphonuclears. The Wassermann test of the blood was negative and the Kline diagnostic test slightly positive. The Kline exclusion test was strongly positive. A lumbar puncture was done, and an initial pressure of 300 mm. of water was found. The Pandy reaction was positive; the cell count was 142, with 92 per cent lymphocytes; the protein content was 191 mg., and the sugar content, 112 mg., per hundred cubic centimeters. The Wassermann reaction was negative with all dilutions. The mastic curve was 1221100000. Cultures and guinea pig inoculations did not show tuberculosis.

The patient recovered consciousness on July 31, 1928, but remained disoriented and somewhat incoherent. Weakness of the left facial nerve was noted subsequently. On August 14 the spinal fluid showed a strongly positive Wassermann reaction with 0.5 and 1 cc. of antigen. After four preliminary injections of iodobismitol with saligenin he was given three typhoid chills, with slight improvement. He was then inoculated with malaria, having ten satisfactory paroxysms terminated with quinine. Spinal puncture on September 20 was followed two hours later by a convulsion. The spinal fluid showed a pressure of 90 mm. of water; the dynamics were normal; the cell count showed 4 lymphocytes per cubic millimeter; the Pandy reaction was positive; the protein content was 47 mg. per hundred cubic centimeters; the mastic curve was 2211000000, and the Wassermann reaction was negative with 0.1 cc. and slightly positive with 0.5 cc. of antigen.

DISCUSSION

DR. G. W. BINKLEY: This man was hit on the head by a golf ball about a week before coming into the hospital. While he apparently recovered in a few hours, I feel that this trauma may have resulted in the convulsions and coma that came on some days later. I feel that the diagnosis of neurorelapse can be questioned. If syphilis is responsible for his symptoms, one would expect more definite findings in the spinal fluid. Even now the findings are not as strongly positive as one would expect in a neurorelapse with clinical symptoms of such severity. I believe that the factor of trauma should not be lost sight of.

DR. J. R. DRIVER: It is interesting to note that there was a reversal to normal of the spinal fluid after about half of the total amount of treatment had been given—that is, after about fifty injections of arsenic and the bismuth preparation. Treatment had been continued, and the negative serologic changes perhaps gave a false sense of security. One should not lose sight of the fact that the patient still has involvement of the central nervous system. It points out one good lesson, namely, that any patient with involvement of the central nervous system should be given the advantage of fever therapy. Had this man been given such therapy at the end of a year of treatment, I think it may be assumed that his present difficulties might have been averted. Therefore, any patient who has had neurosyphilis should receive fever therapy, no matter if a reversal to normal should result from chemotherapeutic methods.

DR. H. N. COLE: Given a man who has had a positive spinal fluid at the inception of the disease and then has sterile spinal fluid—this would not be sufficient to rule out further difficulty as far as the central nervous system is

concerned. It is unfortunate that a lumbar puncture was not made before the onset of this attack. I was much interested in Dr. Binkley's remarks and agree with Dr. Driver. Trauma may have caused the onset. In a large group of cases tabes, dementia paralytica, or some kindred disease has developed as a result of trauma. I agree with Dr. Driver that this case demonstrates the necessity of giving every patient with involvement of the central nervous system the advantage of fever therapy.

DR. R. E. BARNEY: I understand that this man has a definite weakness on one side. This would point to vascular involvement.

DR. W. F. SCHWARTZ: I agree with Dr. Barney that when there are localizing signs of paralysis one is justified in assuming that there is a vascular element as well.

NOTE.—Because of marked mental deterioration the patient was transferred to the psychopathic department of the Cleveland City Hospital on Oct. 5, 1938. Subsequent lumbar punctures have shown considerable variation in the degree of positive findings.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

N. N. EPSTEIN, M.D., *President*

Sept. 30, 1938

H. V. ALLINGTON, M.D., *Secretary*

A Case for Diagnosis (Boeck's Sarcoid and Lupus Erythematosus?).
Presented by DR. A. E. INGELS.

L. H. B., a white salesman aged 51, entered the dermatologic clinic of the Stanford University Hospital on Aug. 2, 1938, because of tumor-like infiltrations as well as more superficial plaques on his face. The first lesion developed behind the right ear in 1930. Since then others have gradually appeared, most numerous on the cheeks and the lower part of the forehead. At present the eyebrows are almost completely replaced by the process. Recently the face has shown more diffuse erythema, and the original sarcoid-like areas have become less distinct. The whole face now shows some edema.

The left leg shows scarring from old varicose ulcers which began in 1935 and are still active.

The patient's general health has been good. Aside from the cutaneous lesions, repeated physical examination has shown nothing abnormal.

The basal metabolic rate is +10 per cent. Repeated Wassermann tests have been negative. Urinalysis gave normal results.

A blood count on September 30 showed: erythrocytes, 4,500,000; hemoglobin, 94 per cent (13.6 Gm.), and leukocytes, 7,300. The differential count showed: polymorphonuclear leukocytes, 37 per cent; lymphocytes, 25 per cent; large monocytes, 6 per cent, and eosinophils, 32 per cent. A blood count on August 22 showed: erythrocytes, 4,800,000, and hemoglobin, 14 Gm. The differential count showed: polymorphonuclear leukocytes, 34 per cent (15 per cent banded); eosinophils, 42 per cent; basophils, 2 per cent; monocytes, 3 per cent, and lymphocytes, 19 per cent.

Roentgenograms of the chest showed the basal shadows to be within normal limits. There were some calcification at the hilus of the right lung and a moderate increase in the bronchial vascular markings in the pulmonary fields, which are of doubtful significance. There was no roentgen evidence of active pulmonary disease.

Repeated examinations of nasal scrapings and smears from the ulcer of the leg for Bacillus leprae have given negative results, as has a leprin test.

Microscopic study of sections taken from a lesion on the left cheek showed moderate hyperkeratosis, plugging of the hair follicles, thinning of the epidermis and, in places, atrophy. In the cutis there was a nonspecific round cell infiltrate around the dermal appendages and blood vessels. Deeper in the cutis was a cell infiltrate containing aggregations of foam cells in a lobular arrangement which suggested sarcoid. Tubercles were absent. None of the sections showed acid-fast organisms.

Past treatment has included many injections of sodium gold thiosulfate and a bismuth preparation. During the past summer the patient received a preparation of arsenic, to which he reacted with articular pain and nausea. Solid carbon dioxide has been applied to the lesions, with some benefit. Removal of teeth, indicated by dental roentgenograms, resulted in no improvement. Recently he has received five intramuscular injections of bismuth subsalicylate. The eruption has been apparently more acute in the past two weeks.

This case is presented because both clinically and histologically there are features of both lupus erythematosus and sarcoid and because of the relative lack of response to treatment. A case of similar involvement was presented previously (ARCH. DERMAT. & SYPH. **32**:311 [Aug.] 1935; **32**:987 [Dec.] 1935; **34**:140 [July] 1936).

DISCUSSION

DR. HARRY E. ALDERSON: When I first saw this patient, at the Veterans Administration Facility, he had definite lesions of lupus erythematosus and elevated plaques that were clinically sarcoid. An interesting development is the loss of hair and eyebrows, which suggested leprosy. I feel that he may have hypothyroidism.

I found early that he was extremely sensitive to arsenic. He told me this, but I did not believe it. When small doses of arsenic were given without his knowledge, he showed symptoms of intolerance to arsenic but no cutaneous lesions.

DR. H. J. TEMPLETON, Oakland, Calif.: I suggest one of the conditions that produce erythema of the face, nodulation and loss of eyebrows; i. e., leukemia cutis or lymphoma of the face.

DR. A. E. INGELS: Dr. Templeton's remark is interesting to me because clinically such a diagnosis as leukemia was considered. At no time, however, has there been any evidence of leukemia in the blood or sections or in the excised glands.

Tuberculid (Acnitis). Presented by DR. N. N. EPSTEIN and DR. E. A. LEVIN.

J. B. O., a white man aged 38, has a fairly extensive yellowish brown papular eruption on the cheeks and forehead. It has been present for eight months and causes no symptoms. Complete investigation by an internist has revealed no evidence of tuberculosis.

A blood count, a Wassermann test of the blood and a urinalysis have given negative results, as has an intradermal test with a 1:1,000 dilution of old tuberculin. A roentgenogram of the chest showed no abnormality. Results of histologic examination were consistent with a diagnosis of tuberculid.

The patient has been given six treatments with unfiltered roentgen rays (75 roentgens each) and has received eight doses of 0.45 Gm. of neoarsphenamine.

There has been great improvement, but new papules continue to develop.

DISCUSSION

DR. L. R. TAUSSIG: Some months ago I saw the microscopic section from one of this patient's lesions. It showed a typical tuberculous arrangement. I agree with the diagnosis of tuberculid more because of the pathologic picture than because of the clinical appearance.

Naevus Verrucosus Linearis, Showing Involution under Treatment. Presented by DR. A. E. INGELS.

A. L., a white Italian waiter aged 28, was first seen on Aug. 8, 1938. At the age of 2 years the patient had a broad verrucous linear nevus on the entire inner surface of the right thigh. A similar condition was present on the right little finger and the ulnar half of the right hand. The lesions on the thigh involuted spontaneously at the age of 4½ years. They recurred in 1932, at the age of 22. Local treatment with salves and ultraviolet light caused them to disappear again. They reappeared in 1937. The lesions on the hand have persisted throughout, though at times they are less marked. There has been severe itching, more noticeable recently.

Local keratolytic applications and weekly doses of unfiltered roentgen rays (75 r) have caused the lesions to involute to the extent of about 75 per cent. The appearance has changed from that of lichen planus hypertrophicus to the present noninflammatory form.

Some of the lesions on the right hand, treated by electrodesiccation, showed a tendency to heal, with an undesirable amount of scarring.

Microscopic study confirmed a diagnosis of verrucous nevus.

A Case for Diagnosis (Trophedema?). Presented by DR. ERVIN EPSTEIN, Oakland, Calif.

E. T., a Negress aged 48, was first seen on June 1, 1938. She stated that when she was 3 years old her mother had noted a dark spot on her left side, which has been slowly enlarging ever since. At 10 years this spot was measured and was found to be 3 inches (7.5 cm.) long and 2 inches (5 cm.) wide. This lesion has always followed the cutaneous surface innervated by the left tenth dorsal nerve. In 1936 a similar area appeared under the left breast and rapidly spread to the back. At approximately the same time a third lesion appeared, in the left lower quadrant of the abdomen. This has shown little extension. The original lesion was asymptomatic until the appearance of the other two. Since then the patient has noted a dull, aching pain and numbness in the actively progressing areas.

Her past history is replete with serious illnesses, including scarlet fever, peritonitis, nephritis, pneumonia, "rheumatism" and laryngitis persisting for six months, and she underwent pelvic laparotomy with "removal of most of her organs," hernioplasty and a sinal operation and was injured seriously in an automobile accident. She has also been treated intermittently for scoliosis. At present she has unilateral headaches and momentary losses of consciousness. There is an indefinite history of syphilis, although numerous tests of the blood have given negative results.

Her cutaneous condition shows that the skin innervated by the left tenth dorsal nerve is greatly retracted, which causes a deep depression in the surrounding obese tissues. This process extends from the vertebral column to a point in front of and above the anterior superior spine of the ilium. Similar areas are present under the left breast extending to the back, and in the left lower quadrant of the abdomen. When the adjacent tissues are separated, the lesions can be seen to consist of smooth shiny hyperpigmented bands of hardened skin. Surrounding induration can be felt extending for several centimeters on each side and beyond each extremity of the visible lesions. The palpable lesions are somewhat tender; the visible ones are not. The lesions are hyperesthetic. Surgical scars, vaccination scars and striae fail to show any hypertrophic tendency. There is no history of preceding trauma, local infection or herpes zoster.

The patient was referred to the outpatient department of the University of California Hospital in July and was carefully studied in the departments of internal

medicine, dermatology, neurology, urology and endocrinology without the discovery of any further significant information. All laboratory tests, including blood counts, urinalyses and serologic tests, gave results within normal limits. The basal metabolic rate was —1 per cent. Subcutaneous injection of 1 per cent congo red did not show amyloidosis.

Histologic study of the original lesion and one in the left lower quadrant of the abdomen showed principally edema of the epidermis and swelling and separation of the collagen bundles.

DISCUSSION

DR. G. V. KULCHAR: I think this patient has a sclerosing type of panniculitis.

DR. F. G. NOVY JR., Oakland, Calif.: No roentgen studies of the genitourinary tract have been made. I still think that she may have some low grade pathologic

Gigantism of one finger in an infant.

changes in the region of the left kidney or in the peritoneal cavity. There is extreme tenderness over the involved area.

DR. ERVIN EPSTEIN, Oakland, Calif.: I feel that histologically the sections resembled scleredema adultorum. Of course, that diagnosis does not fit clinically. Sections were sent to Dr. Hamilton Montgomery, Rochester, Minn., who expressed the belief that the microscopic picture is compatible with a diagnosis of scleredema adultorum. The lesions follow the distribution of the left fifth, tenth and twelfth dorsal nerves. All factors considered, I believe that the patient has trophedema on the basis of pathologic neural change.

Gigantism of One Finger in an Infant. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

W. C., a boy aged 8 months, has an enlargement of the left third finger. It was first noted at birth, and growth has been only minimal since then.

The appearance of the finger and nail is normal for a child about 12 years of age except for a slight bluish tinge of the subcutaneous tissue. It has been sug-

gested that this represents the hypertrophy occasionally seen in an extremity where there is deep angioma or arteriovenous anastomosis.

Roentgen examination showed normal but enlarged bones.

DISCUSSION

DR. EUGEN OSTWALD (by invitation): I should like to ask whether there is any disturbance of the endocrine system. In some cases of gigantism reported in the literature the condition is associated with dysfunction of the pituitary gland. In some an actual enlargement or tumor of this gland has been proved. May I suggest that a roentgenogram of the skull, especially of the sella turcica, be taken if that has not yet been done?

DR. H. J. TEMPLETON, Oakland, Calif.: It has been suggested that the finger should be removed. However, I think it should be left alone for a year or two to see whether the other fingers overtake it in growth.

Melanoma of the Right Eye. Presented by DR. FRANCES TORREY.

A. L. H., a white housewife aged 47, has an area of deep brown pigmentation. It is roughly crescent shaped, involving the right conjunctiva, medial to and below the cornea. It measures approximately 10 by 18 mm. This has been present for about twenty-eight years.

Physical examination gives otherwise negative results. Urinalysis showed no melanin.

Malignant Melanoma of the Right Eye. Presented by DR. L. R. TAUSSIG.

S. R., a white housewife aged 48, has an area of deep brown pigmentation of the right eye, involving the caruncle, both the skin and conjunctival surfaces of the lower lid and the outer and inner fornices of the upper lid. It has been present about three years. The patient attributes the stain to the use of mild protein silver.

Physical examination showed no abnormality except an enlarged heart with a soft diastolic murmur. There was no evidence of metastasis.

The urine showed no melanin.

DISCUSSION

DR. STUART C. WAY: The question arises whether the pigmentation in the first patient represents a benign or a malignant condition. Its long duration without change suggests the term "melanoderma" rather than "melanoma."

DR. MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: I think it is a mistake to call such a lesion a melanoma, because such a term suggests malignancy. Pigmented nevi of the conjunctiva are rare. Pigmented hairy nevi are still more uncommon. I saw such a lesion on the cornea of a patient several years ago.

DR. L. R. TAUSSIG: I was particularly interested in the type of treatment advisable. These 2 cases present different problems. I believe that the nevus or melanoma on the ocular conjunctiva is potentially malignant; however, since it has remained practically quiescent for at least twenty years, I feel that no treatment is indicated.

The other patient's lesion has increased progressively. It extends to and involves the caruncle. I think that radical operation would give some chance of cure.

The decision as to whether a melanoma is malignant must be based on the clinical appearance, the course and the microscopic picture. I have removed a number of moles that seemed quiescent and have been told that histologically they were malignant. On the other hand, I have removed clinically malignant lesions which pathologists said were nonmalignant. I do not believe that microscopic examination alone can determine whether a lesion is or is not malignant.

Scleroderma. Presented by Dr. H. V. Allington, Oakland, Calif.

J. H., a white man aged 59, has been followed for the past three months in the dermatologic clinic at the Alameda Health Center. About two and one-half years ago he first noted swelling of the hands and knees. As this gradually subsided, the areas became "stiff and woody." Gradually the process has become generalized. At present the patient has a masklike, expressionless facies. His hands are held in a neutral position and have a waxy, semitranslucent appearance. On the knuckles and interphalangeal joints the tissues are white and show varying degrees of necrosis from pressure and ischemia. There are scattered morphea-like areas of depigmentation alternating with increased pigment on the backs of the hands. The skin over the whole body is infiltrated, unyielding and rigid. This condition is most noticeable on the hands, where it has progressed to a point where the thumbs and the third and fourth finger tips cannot be opposed. It is becoming difficult for the patient to open his mouth, and there appears to be interference with the swallowing mechanism. Recently a cough has developed, and brownish mucoid sputum is raised with some difficulty.

The patient has had no serious illnesses. He lost his right eye in an accident about twelve years ago. He had a short attack of pleurisy in May 1937. There is no history of familial disease. He has worked in the past as a salesman and car washer.

Blood counts on two occasions have been normal. Urinalysis has given normal results. On May 25, 1938, the basal metabolic rate was —14 per cent. The sputum on September 21 showed no acid-fast bacilli.

For the past four months he has been taking a high caloric ketogenic diet, together with NH_3Cl_2. For the past two months he has also taken 1 grain (0.06 Gm.) of thyroid and 30 minims (1.85 cc.) of viosterol daily. There has been no improvement.

DISCUSSION

Dr. Merlin Trevor-Roper Maynard, San Jose, Calif.: I should like to suggest that the vitamin D be continued. My own experience with vitamin D has been only in localized scleroderma (morphea). In 1 of my patients the lesions cleared up completely; in the other they have almost cleared. Treatment was continued for eight months. I should suggest that the patient be given 100,000 units daily if he can be kept track of.

Dr. A. E. Ingels: During the past year I have treated dermatomyositis with an insulin-free pancreatic extract—the Winthrop compound called "padutin." This is supposed to cause peripheral vascular dilatation. A few reports have indicated that it is of value. In the case referred to the effect was dramatic. Before treatment the patient could hardly walk or eat. The improvement might possibly have been a spontaneous remission, but I think it was due to the use of padutin, since improvement occurred only during the period when it was given.

Dr. Harry E. Alderson: The patient referred to by Dr. Ingels had been bedridden. A few weeks after treatment was begun she was up on crutches. The improvement was striking.

Dr. H. J. Templeton, Oakland, Calif.: I once presented before this group a girl 10 or 12 years old with localized scleroderma of the face, who was treated with extract from the insulin-free portion of the pancreas, with complete recovery (Arch. Dermat. & Syph. **33**:571 [March] 1936; **34**:708 [Oct.] 1936).

Dr. L. R. Taussig: I wonder whether parathyroidectomy might be considered.

A Case for Diagnosis (Insect Bites?). Presented by Dr. Merlin Trevor-Roper Maynard.

H. P., a farm worker aged 36, was seen on September 15, in consultation with Dr. F. P. Rutherford, of San Jose, Calif., at the O'Connor Hospital. The patient states that two weeks prior to his entry to the hospital, while moving tree props,

he encountered many insects as well as nests of rats and squirrels. He felt what he believed were insect bites on several areas of the body, which itched violently afterward. The next day he felt sick and stayed in bed. He felt better in a few days but was weak.

Dr. Rutherford stated that there was general enlargement of the lymph glands with a high lymphocyte count and a 6 to 9 per cent concentration of eosinophils.

Examination showed several discrete, deeply infiltrated vacciniform lesions. One was seen on each forearm, one on the left shoulder, one on the left knee and one on the right hip. They were clinically typical of a severe reaction to an insect bite.

The patient was seen again on September 27, at which time the lesions were much as they are today. A rounded slough was present in the center of each. The lesions were still hard and granulomatous. Weakness was pronounced. A blood count on this day showed: 12,950 leukocytes, with 47 per cent neutrophils, 5.5 per cent eosinophils, 42 per cent lymphocytes and 5.5 per cent monocytes. Agglutination tests for tularemia and Malta fever gave negative results with all dilutions. The following conditions were considered in differential diagnosis: tularemia, bubonic plague, relapsing fever and aleukemic leukemia. Bites by a black widow spider are considered the most likely.

DISCUSSION

Dr. Orland F. Montgomery: I have observed 3 cases in which somewhat similar lesions were due to gnat bites. One woman had eight or ten bullous lesions on the ankles, which were the size of a silver quarter and were multilocular. Subsequently, some underwent central necrosis. All of these patients came from the San Francisco peninsula.

Dr. N. N. Epstein: I question whether a bite by a black widow spider or other insect can take on this appearance five weeks after it occurs. Could the lesion be some type of metastatic mycotic infection? The patient states that he feels ill.

Dr. Stuart C. Way: According to the patient, lesions suggestive of dermatitis herpetiformis have been present in the scalp for many years.

Dr. H. J. Templeton, Oakland, Calif.: Has he had any fever?

Dr. Merlin Trevor-Roper Maynard, San Jose, Calif.: He has previously had sycosis vulgaris. He has had no fever since the first two days, but severe prostration has continued until the past two days.

Subungual Hyperkeratoses. Presented by Dr. H. J. Templeton, Oakland, Calif.

R. B., a white American man aged 52, consulted me two days ago because of subungual hyperkeratoses involving the first and fifth right fingers, the second left finger and the third right toe. These have been present for three months.

Clinically the growths consist of extremely hard material much like that of a cutaneous horn. They are flat; they apparently spring from the nail bed and force the nail plate outward, producing partial onycholysis.

Microscopic examination of this material showed no fungi. Lateral roentgenograms showed no subungual exostoses.

My associates and I have observed a number of similar lesions in the past without feeling certain of their classification.

DISCUSSION

Dr. Merlin Trevor-Roper Maynard, San Jose, Calif.: I believe that these lesions are occupational, secondary to repeated mild trauma. The patient is an accountant. Even the minor injuries received in operating accounting machines could, I believe, be responsible.

Hyperkeratotic Fungous Infection of the Palms and Soles. Presented by Dr. H. V. Allington, Oakland, Calif.

Case 1.—R. L. S., a white man aged 29, presents a fungous infection of the left hand, both feet and several nails. This is said to have begun on the hand about a year ago. The involved areas are hyperkeratotic and show irregular ragged superficial scaling. They include the palm, both soles and the palmar and plantar surfaces of the digits. The dorsal surfaces are not involved. An occasional deep-seated vesicle is seen on the sides of the fingers or interdigital webs. A few painful fissures have occurred, principally about the interdigital webs. The nails show hyperkeratosis of the nail bed with elevation of the nail plate first at the lateral and distal margins.

Abundant mycelium has been repeatedly seen microscopically in horny material removed from the palms, soles and nails. The causative organism has not been identified culturally. The clinical picture is similar to that produced by Trichophyton purpureum in the cases reported by George M. Lewis, Royal M. Montgomery and Mary E. Hopper (Arch. Dermat. & Syph. **37**:823 [May] 1938).

Trichophytin (1:500) produced a mild reaction on intradermal test.

The patient has been continuously treated with fungicidal preparations for the past nine months. At present an ointment containing 10 per cent salicylic acid and 10 per cent precipitated sulfur is being used. This has controlled the infection better than anything previously tried, but it is still active.

Case 2.—L. W. Z., a white man aged 33, presents a fungous infection of the right palm and fingers, of the feet and of several nails, alike in appearance and location to that of the previous patient (R. L. S.). It is said to have begun on the hand three and one-half years ago. Mycelium is easily observed microscopically. Much past treatment has been of only slight benefit.

DISCUSSION

Dr. H. J. Templeton, Oakland, Calif.: For years I have made routine microscopic examination in cases of scaling of the palms, with almost uniformly negative results. Suddenly a half dozen cases have appeared in which the fungi are easily demonstrated.

Dr. A. E. Ingels: In such cases I suggest culture and specific autogenous vaccine treatment. Infections by Tr. purpureum are particularly resistant to treatment.

Dr. Harry E. Alderson: For several years I have been instructing patients with such lesions to cleanse the affected areas with vinegar, and I have found it useful in combination with other measures. During the past year I have been using lemon juice. In my experience it is helpful. Recently I have tried a saturated aqueous solution of citric acid containing 2 per cent salicylic acid. It seems to discourage growth of the fungi.

Intolerance to Heavy Metal. Presented by Dr. Ervin Epstein, Oakland, Calif.

S. P., a 34 year old painter, states that several lesions developed on the tongue and an eruption on the right thenar eminence in September 1937. He visited a general practitioner, who found serologic evidence of syphilis and started treatment by the intravenous injection of neoarsphenamine every five days. The Wassermann reaction of the patient's 22 year old bride of three months was also positive, and she was given identical therapy. After the completion of this course for each patient, bismuth therapy was instituted.

The husband had a sore hip after the first injection and refused further injections into the hip. Therefore he was given an injection of bismuth subsalicylate every five days into the left deltoid muscle. In December, after a few such injections, he showed pigmetation of the gums, severe abdominal cramps and other signs and symptoms leading to a diagnosis of lead poisoning at the Southern

Pacific Hospital in San Francisco. He was hospitalized about a month and was then given neoarsphenamine in doses of 0.6 Gm. every five days until I first saw him, on June 22, 1938.

His wife tolerated the intragluteal injections of bismuth satisfactorily but had some soreness of the mouth and pigmentation of the gums. Despite this, bismuth therapy was continued until severe stomatitis developed in February. Despite cessation of therapy, she noted severe pains in the left leg that, from the history, were probably due to peripheral neuritis, although thrombophlebitis could not be ruled out. These were so severe as to necessitate one month's hospitalization. After this she received the same treatment as her husband.

Both patients reported to my office on June 22. Physical examinations and urinalyses gave negative results for both. Serologic tests of the husband's blood gave negative results, but the reaction of the wife's blood was 4 plus. Bismuth therapy was instituted again. After the first injection the husband's hip became sore, and he insisted on taking the injections in the left triceps muscle. After he had taken two more injections he began to have abdominal cramps and pinpoint-sized pigmented spots on the tongue and gums. Treatment was interrupted, but he continued to have cramps intermittently for the next five weeks. His wife had fairly severe stomatitis after the third injection of the bismuth preparation.

Both were then given neoarsphenamine and took six injections of from 0.3 to 0.45 Gm., without complications. They were each given mercuric salicylate, 1 grain (0.06 Gm.) intragluteally, on September 6. Mr. S. T. had soreness in the hip which forced him to stop working for one day. He refused further intramuscular therapy. Mercury rubs were also rejected. After the first mercurial injection in the right hip his wife noticed numbness of the left leg, and after the second she had severe pains and tenderness in the left leg, which forced her to remain in bed. It was decided to discontinue mercurial injections.

These patients are presented because of the rarity of complications following heavy metal therapy, especially in patients with conjugal syphilis. It is also hoped that some suggestions will be made as to the further treatment of these patients.

DISCUSSION

DR. H. J. TEMPLETON, Oakland, Calif.: I suggest that Dr. Epstein try a 2 per cent solution of colloidal mercuric sulfide. I have found it to be tolerated in several cases of bismuth intolerance. I should give 2 cc. intramuscularly twice a week.

DR. L. R. TAUSSIG: Another possibility would be intravenous mercury.

DR. G. V. KULCHAR: Colloidal mercuric sulfide can be given intravenously also if one has any trouble with intramuscular injections.

DR. ERVIN EPSTEIN, Oakland, Calif.: The woman had peripheral neuritis from injections of both the bismuth compound and the mercury. I was interested in the development, in the man, of lead poisoning along with the reaction to bismuth. Five weeks after the last injection of the bismuth preparation he was still having abdominal cramps. While he was given no bismuth (from January to June) he had no trouble. Apparently the symptoms were due to the replacement of lead in osseous deposits by bismuth.

He had abdominal cramps more severe than any I have previously seen from bismuth. He was exposed to both bismuth and lead, but he was given only three injections of the bismuth compound. These symptoms are certainly more common as a result of plumbism than of intolerance to bismuth.

DR. G. V. KULCHAR: I doubt if so few injections of a bismuth preparation would cause a bismuth line.

DR. ERVIN EPSTEIN, Oakland, Calif.: Clinically the pigmentation does not look like a bismuth line.

DR. E. A. LEVIN: Recently I saw a patient who after only the third injection of bismuth subsalicylate had a rather severe reaction, with pigmentation, stomatitis and gingival ulceration.

DR. N. N. EPSTEIN: There are certainly different types of reaction to bismuth. Some patients are highly sensitive and will have severe stomatitis after one or two injections, while others show a similar condition only after many injections of the drug.

Hidradenitis Suppurativa. Presented by DR. N. N. EPSTEIN and DR. E. A. LEVIN.

R. H., a white woman aged 25, for the past five years has had recurring indolent nodules which break down and discharge purulent material. They involve the axillas and the perianal areas.

The patient has not been free of active lesions, although some have healed, leaving noticeable scars. Others are in various stages of healing.

The blood count and the results of urinalysis were normal. The Wassermann reaction of the blood was negative.

Microscopic examination of smears and culture showed a mixture of staphylococci and streptococci. Microscopic sections showed a subacute (apparently pyogenic) inflammatory reaction.

Treatment has included seven roentgen ray treatments, unfiltered, of 60 r each. Intramuscular injections of boiled milk (lactigen) were given. Solution of potassium iodide and viosterol have been taken by mouth. A slow but noticeable improvement has resulted.

DISCUSSION

DR. HARRY E. ALDERSON: It is interesting that this process shows acute exacerbations at the close of the menstrual period and the lesions are in locations where apocrine glands are numerous.

DR. H. J. TEMPLETON, Oakland, Calif.: The last patient I had recovered while receiving filtered roentgen irradiation and subcutaneous injections of staphylococcus ambotoxoid (Squibb).

DR. STUART C. WAY: When the involved area in the axillas is not too extensive, complete excision seems to be the method of choice.

DR. MERLIN TREVOR-ROPER MAYNARD, San Jose, Calif.: Recently acute lesions cleared at once when sulfanilamide was given.

LOS ANGELES DERMATOLOGICAL SOCIETY

KENDAL FROST, M.D., *Chairman*

Oct. 11, 1938

CHARLES R. CASKEY, M.D., *Secretary*

Chronic Oral Moniliasis (Thrush). Presented by DR. SAUL S. ROBINSON.

H. S., a white girl aged 7 years, presents numerous white, glistening flaky lesions on the buccal, lingual and sublingual mucous membranes. The lesions are easily detached. Cultures on dextrose agar and Sabouraud's medium showed a pure growth of Monilia albicans. The patient has been treated for the past two years without any appreciable improvement. Sodium bicarbonate, methylrosaniline (gentian violet) and silver nitrate solutions have been tried. At present she is being treated with an autogenous vaccine made from M. albicans.

DISCUSSION

DR. L. F. X. WILHELM: It will be interesting to see the patient in one or two months, after she has had more vaccine treatment.

DR. SAMUEL AYRES JR.: I should like to know what strength gentian violet was used. I suggest a 5 per cent solution and a mouthwash of compound solution of iodine, 1 teaspoonful in a glass of water. I think both preparations will be of benefit. Such conditions are not always as easy to clear up as the statistics suggest.

DR. HARRY P. JACOBSON: I hesitate to question the presenter's diagnosis, but I feel that it is not justified. The mother states that the condition appeared when the child was 2 years old and that the lesions today look the same as they did when she first observed them. Examination of the patient tonight reveals fairly extensive involvement of the buccal and sublingual mucosa by fairly marginated slightly elevated leukoplakia-like plaques which on close inspection are seen to be somewhat thickened and here and there are verrucous and closely adherent to the underlying mucosal surfaces. There is no evidence of inflammatory reaction in or about any of the patches. In view of this history and of the appearance of the lesions, I do not feel justified in subscribing to a diagnosis of moniliasis.

The isolation of a monilial organism from lesions in the girl's mouth is not sufficient justification for a diagnosis of moniliasis. Monilia are fairly common normal inhabitants of the mouth, and in this case they probably are secondary saprophytic invaders. I believe the eruption represents a congenital defect of some kind or possibly a nutritional disturbance due to avitaminosis B. I do not believe that treatment with monilial vaccine will solve this problem.

DR. CHARLES R. CASKEY: I agree with the diagnosis of monilial infection. I think it is possible that M. albicans can in some instances produce pathologic changes. The same thing is true of Vincent's organisms.

DR. KENDAL FROST: These lesions recall those in the case which I presented before this society some years ago and later published (Frost, K.; Sutherland-Campbell, H., and Plunkett, O. A.: Monilia of the Tongue, ARCH. DERMAT. & SYPH. **20**:811 [Dec.] 1929). The patient was a man and presented a problem of dietary deficiency as well as the oral lesions of monilial infection.

DR. SAUL S. ROBINSON: In answer to Dr. Ayres's question, compound solution of iodine and 5 per cent gentian violet have been used for a number of months, without any relief. At present autogenous vaccine has been made up with 56,000,000 organisms per cubic centimeter. I am starting with small doses, and I shall be glad to report later on the response. The condition seems to me to be chronic thrush. The lesions do not remain in one area, as a nevus would do. I have photographs taken when the lips were involved. Today they are free of the disease. That would settle the diagnosis of nevus.

A Case for Diagnosis (Lichen Planus?). Presented by DR. JULIUS R. SCHOLTZ.

M. L., a white man aged 22, has an eruption the primary lesions of which are dull red solid flat-topped papules beginning at about the size of a pea. A few remain single, but most of them have aggregated into large patches, which tend to be round but in some instances suggest a serpiginous outline. Several of the large lesions have clearing centers which produce an annular configuration. The lesions at first were smooth and soft, but under roentgen treatment they have begun to show a dry, fine adherent scale. The lesions have at all times been definitely indurated. They are located predominantly on the extensor surfaces of the arms and legs, with major groups around the elbows and knees. There were plantar lesions which clinically appeared to be mycotic and which cleared under appropriate treatment. Serologic tests for syphilis gave negative results. A pathologic section did not show a diagnostic picture. The granular layer showed some increase in thickness, but the major changes were in the corium, which was moderately infiltrated with round cells. The lesions are subsiding under fractional doses of roentgen rays. Ointments seem to be irritating.

DISCUSSION

DR. CHARLES R. CASKEY: I suggest the possibility of tinea.

DR. JULIUS R. SCHOLTZ: The prime reason for presenting this case is that it illustrates the dynamics of cutaneous morphology. The first time I saw the lesions I felt as Dr. Caskey does, that they were due to an ordinary mycotic infection. Several days later, however, they became slightly indurated and dull red and suggested a late relapsed type of cutaneous syphilis. Finally a glossy surface appeared and the induration increased; dry adherent scales appeared, and the diagnosis of hypertrophic lichen planus seemed correct.

Porokeratosis (Mibelli). Presented by DR. JULIUS R. SCHOLTZ.

S. S., a white man aged 42, presented in October 1937, is shown to demonstrate the result of treatment and the appearance of two new lesions. The treated lesion in the left pectoral region is still visible, but has changed somewhat in appearance. One superficial electrodesiccating treatment was given to the active edge. Several months later the lesion showed definite flattening and disappearance of the light brown color. A small keloidal nodule has developed in the site from which material for biopsy was taken; the remainder of the lesion is white and flat, but the margin still shows a palpable threadlike boundary. The lesion is evidently inactive. Several months ago two pea-sized lesions appeared over the sacral area. These show definite brownish coloration, slightly atrophic centers and a fine raised border which has begun to show the pearly color characteristic of the lesion. I should like to point out that treatment is only moderately successful so far as appearance is concerned, because of the tendency to keloid formation. However, treatment by electrodesiccation seems to prevent progression of the lesion.

Porokeratosis (Mibelli). Presented by DR. SAMUEL AYRES JR. and DR. NELSON PAUL ANDERSON.

P. D., a white girl aged 18, states that she first noticed an eruption on the arm, near the elbow, about eight years ago. The lesion was believed to be ringworm and was treated as such, without benefit. One area was treated with some kind of acid, after which a small keloid developed. Two new lesions, both annular, have occurred in the same area. For four or five years several small lesions have been present on the back of the right elbow. There have been no subjective symptoms. At present the patient shows three annular serpiginous lesions, more or less confluent, near the left cubital fossa. The borders are narrow, raised, sharply defined and erythematous and show a hyperkeratotic ridge or disk at the summit of the border, apparently made up of separate tiny corneous plugs. The centers are slightly depressed and show definite atrophy, which has developed spontaneously. There are two pinhead-sized lesions on the flexor aspect of the left forearm and two on the posterior aspect of the right elbow. There are two navy bean–sized keloids in the area of greatest involvement, one marking the site of a recent removal of tissue for biopsy, the other marking the area previously treated with acid.

Sections of the tissue show the epidermis and the corium. Through the center of the specimen was a funnel-shaped defect extending through the epidermis and lined on both sides by a thickened layer of stratified squamous epithelium. It was filled with an exudate of polymorphonuclear leukocytes and contained hyaline fibers which had apparently migrated into this area from the underlying corium. The inflammatory exudate extended for a short distance into the corium, and nodules of round cells were present about the deeper cutaneous appendages. At one margin of the lesion described there was an oval plaque of cellular fibrous tissue in the papillary layer of the corium. The surface of the entire specimen was covered with squamous epithelium, with a thick layer of squamous epithelial scales.

DISCUSSION

DR. SAMUEL AYRES JR.: Since the eruption of our patient has shown little improvement after treatment with solid carbon dioxide, after seeing Dr. Scholtz's patient, I think it might be well to try electrodesiccation in one area and see the

result, although we have refrained from the use of electrosurgical methods in this case because of the keloidal tendency of the patient. The keloids are being treated with fractional doses of roentgen rays.

A Case for Diagnosis (Lymphoblastoma Cutis? Lymphogranulomatosis?). Presented by DR. KENDAL FROST.

G. B., a white man aged 38, was shown to this society on May 11, 1937. His eruption is of two years' duration. The lesions are scattered fairly symmetrically over the body. On the trunk they are discrete infiltrated superficial erythematous round and oval, varying in size from that a split pea to that of a bean, with white silvery scales on some of them. These are more marked on the flanks, on the upper half of the abdomen, in the axillas and on the flexor surfaces of the arms. On the sacrum is a roughly triangular area of lichenification and brownish pigmentation, and in it are some excoriations. On the knees there are fairly well circumscribed erythematous and scaling patches about 3 by 10 cm., with moderate infiltration. The palms and soles present thickened hyperkeratotic areas. There is no appreciable scaling between the toes. The palms are diffusely thickened. The inguinal glands are palpable but not greatly enlarged. The epitrochlear, cervical and axillary glands are palpable and the latter a little larger than normal. The blood count on May 24 was normal except for an eosinophil count of 4 per cent. The count on May 23 showed no appreciable changes. The pathologic section, made March 15, showed benign lymphoid hyperplasia and a nonspecific inflammatory lesion of the skin. These were reported at the last showing of this patient.

Application of antipruritic lotions and a few roentgen treatments caused temporary disappearance of the lesions. On Sept. 6, 1938, he was given 150 roentgen units of unfiltered radiation to the palms, which brought about improvement.

DR. WILLIAM H. GOECKERMAN: The diagnosis, I think, must remain undecided. I personally feel that, as the disease is of two years' standing or more, and the patient is still in good condition, it is not Hodgkin's disease unless the response to treatment has been exceptional. Of course, if systematic roentgen treatment has been carried out, the problem is different. Even then, in the average case there should be farther advanced symptoms, glandular involvement and lesions.

DR. JULIUS R. SCHOLTZ: I had the opportunity of seeing this patient in Dr. Frost's office in daylight and was of the opinion that the condition was superficial mycosis, with a question of contact dermatitis. It seems unlikely that the patient would be in such good general condition two years after a diagnosis of Hodgkin's disease, even granting that he has had excellent radiation therapy. Statistics seem to indicate that although irradiation makes life more livable, it does not prolong it.

DR. SAMUEL AYERS JR.: In the absence of any definite proof of lymphoblastoma, I think one should consider hyperkeratotic eczema, probably associated with vitamin deficiency.

DR. KENDAL FROST: The lesions on the hands and feet have been a recent development. Early this spring the lesions on the body were suggestive of pityriasis rosea but were of much longer duration than is usual in that disease. The lesions on the hands have improved at least 75 per cent in the last month, since he was given 150 r (½ skin unit) of roentgen rays. He has always had mild chronic dermatophytosis between the toes, but no more than one sees in the average person in his class. There has never been any vesiculation on the feet. The lesions are chiefly on the pressure surfaces of the heels and the mesial surfaces of the soles, under the big toes. There is a large varicosity running the length of one leg, and over that entire area is an elongated patch of dry erythema. It seems to me that the recent lesions which he is manifesting are perhaps appearing in places of lowered local resistance due to pressure or circulatory disturbance. I feel that there will ultimately be changes characteristic of one of the group of lymphoblastomas, probably mycosis fungoides, but it may take considerable time before a definite diagnosis can be made.

CHICAGO DERMATOLOGICAL SOCIETY

HAMILTON MONTGOMERY, M.D., *President*

Oct. 21, 1938

H. RATTNER, M.D., *Secretary*

A Case of Nevoxanthoendothelioma. Presented by DR. E. A. OLIVER.

A boy aged 7 months has had lesions since the age of 6 weeks. These lesions looked then much the same as they do today, with the exception of the crease or fissure lateral to the larger lesion, which is due to treatment by electrolysis.

On the left side of the ala nasi is a grape-sized yellowish brown lesion. It is shiny and tense, with delicate telangiectatic vessels coursing over it. Lateral to it are three smaller similar lesions. There are no subjective symptoms.

DISCUSSION

DR. OLIVER S. ORMSBY: For the past two years I have been seeing a patient with a condition that fits in with the juvenile xanthoma group. I have seen that patient within two or three days, and the picture is so different from this one that it seems they should hardly be considered examples of the same disease. While the condition has improved, the child still has an extensive eruption. The lesions are less yellow and are flatter, and possibly a few have disappeared, but they are still prominent. In nevoxanthoendoepithelioma the lesions are few (two, three or half a dozen), but the condition never occurs as a generalized eruption such as was seen in the case mentioned. While there are histologic resemblances between the two they can be differentiated.

In going over a number of records of juvenile xanthoma, I found that at least 20 or 30 patients whose cases were reported during infancy still had lesions at 25 or 30 years of age, while all the eruptions like the one in this case had completely disappeared.

The clinical appearance and course are also different, the one having a few lesions which undergo involution in time and the other often having extensive lesions which remain indefinitely. A. B. McGraw (*Am. J. Cancer* **18**:345 [June] 1933) recorded a number of cases of adults with xanthoma which began in childhood.

DR. MARCUS R. CARO: I think that the picture fits into the group described as nevoxanthoendothelioma, or juvenile xanthoma.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I believe that this case is one of nevoxanthoendothelioma. Histologically there are typical endothelial giant cells as well as Touton giant cells and a few typical xanthoma cells. There is more fibrosis than in the usual case, but I think this simply indicates that the process is beginning to undergo involution. Nevoxanthoendothelioma starts in infancy. The lipoid content of the blood is normal, and the lesions undergo involution spontaneously after a period of months or at most a few years.

DR. E. A. OLIVER: When I first saw this child I was struck with the similarity of the lesion to nevoxanthoendothelioma and juvenile xanthoma. There appear to be two or three lesions, but only one has been tampered with surgically, making it appear to be a group of lesions. Histologic examination showed many of the features of nevoxanthoendothelioma, and although only one lesion is present, I presented the case today as one of nevoxanthoendothelioma.

A Case for Diagnosis (Chronic Vegetative Dermatitis with Scleroderma-tous Lesions). Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

J. B., a white woman aged 36, was first seen at the University of Chicago Clinics on Aug. 6, 1938.

The changes began six years ago on the left toes with fissuring associated with pruritus. While there was temporary improvement, especially in cold weather, the condition has been progressing steadily, with gradual involvement of all the left toes, then four years ago of the right toes and two years ago of the soles and sides of the feet. For six months she has noted lesions on the wrists. The lesions are pruritic and tender.

General examination showed no abnormality. The blood pressure was 136 systolic and 98 diastolic. The Wassermann and the Kahn reaction of the blood serum were negative, and the urine was normal. Microscopic examination of the lesions of the feet showed no fungi.

Examination of the feet shows a polymorphous eruption covering the aforementioned areas and consisting of vesicles, dry vegetations and keratotic lesions. At the sides of the feet there are also white thickened lesions 0.5 to 1 cm. in length. The nails are thickened and discolored. On the wrists there are atrophic lesions 3 to 5 mm. in diameter.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: I was impressed with the character of the lesions on the wrists, which were flat-topped, polygonal papules of the type of lichen planus. Accordingly, I felt that the atrophic lesions might well be the remnants of lichen planus.

DR. OLIVER S. ORMSBY: Dr. O'Leary's comment recalls a point of confusion between lichen planus sclerosus et atrophicus of Hallopeau and ordinary lichen planus with atrophy. The lesions of the former are flat-topped, irregular white papules having black, horny spines on their surfaces. No red or brownish red papules of lichen planus are present. In a limited number of cases of ordinary lichen planus, atrophy sometimes occurs in some of the papules.

DR. H. R. FOERSTER, Milwaukee: I did not make a diagnosis in this case, but I considered lupus erythematosus and lichen planus, favoring the former because of the hyperkeratotic plugs and scales and atrophy within areas of dermatitis. I failed to see the lesions on the wrists.

DR. M. H. EBERT: I was inclined to think it was lichen planus atrophicus et sclerosus. The distribution of the lesions is certainly extraordinary. It is something new in my experience. However, it is a good illustration of the fact that a lesion of any kind is greatly modified when it occurs on the plantar surface.

DR. CLARK W. FINNERUD: There is also much crusting on the webs and dorsal surfaces of the toes. I wonder if Dr. Becker had any particular explanation for that portion of the eruption. My first impression was that the generalized eruption was lichen planus atrophicus, and I still believe it to be an unusual example of this disease. I found one small lesion, about the diameter of a French pea, that seemed to be slightly sclerotic on palpation. I noted the lesions on the wrists.

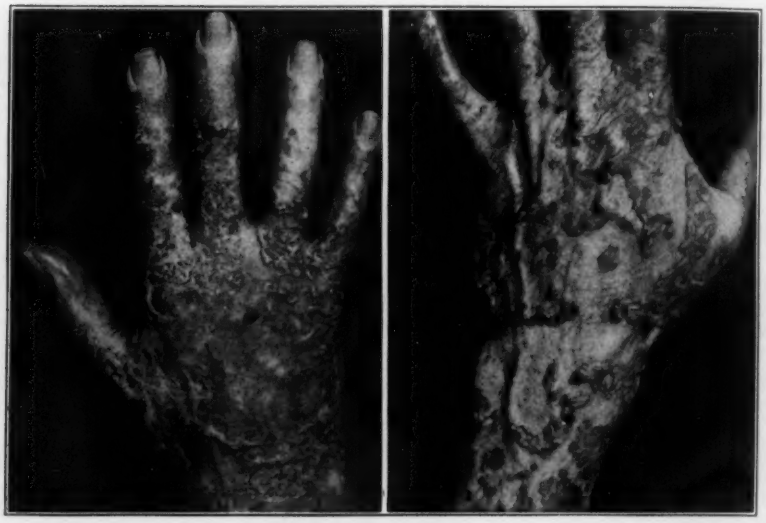
DR. S. W. BECKER: I saw this patient for just a few minutes some months ago; she was Dr. Obermayer's patient. I put her on the list for this meeting because the condition was obviously unusual. I have no particular diagnosis to offer. We took sections from the hyperkeratotic lesions, but unfortunately they did not turn out well. The scleroderma-like lesion from the section we have, which is not entirely satisfactory, is not unlike that described for white spot disease, but the distribution of the lesions is not in conformity with that diagnosis.

A Case for Diagnosis (Pyoderma?). Presented by DR. E. A. OLIVER.

The patient is a white man aged 60, who is an inmate of the Veterans Administration Facility. He states that in 1934 he abraded the skin on the proximal phalanx of the left little finger. The next day he observed an inflammation about the wound, which rapidly spread to the dorsum of the hand and over the dorsal aspect of the wrist to involve the lower third of the forearm. He described the lesion as an inflammatory reaction with formation of localized areas of slightly raised papules along an advancing border. These papules soon became pustular

and broke down, leaving a draining sinus. This infection finally subsided after about one and a half years. He had no further trouble until March 1937, when he noticed a pustule on the radial aspect of the right wrist. He broke this accidentally, and the infection spread under the skin in the same manner as the former lesion had spread on the left hand. When I first saw him the infection involved the right index and little finger and the upper third of the forearm. He complained of pain and tenderness. There were induration, inflammation and pus formation in localized areas and on the side of the right forearm; in its upper third was another area of deep-seated cellulitis containing several oozing sinuses. The infection has now entirely disappeared after treatment with warm boric acid compresses and ammoniated mercury ointment.

The Wassermann reaction was negative, and examination of the blood showed it to be normal. Cultures of pus on Sabouraud's medium were negative for Blastomyces. Hemolytic streptococci and Staphylococcus albus were found. On blood agar a hemolytic streptococcus and a gram-negative bacillus were found.



Unusual form of pyoderma.

DISCUSSION

Dr. Lester M. Wieder, Milwaukee: I think this condition might be the end result of an unusual form of pyoderma with destruction comparable to that produced by acne conglobata. Apparently the tissues have been so undermined and extensively involved as to give the bizarre appearance present. I am at a loss to explain the etiologic organism, to which the patient's tissues must be highly allergic. It is also difficult to account for the restricted localization over such a protracted period, in view of the probability that its spread has been largely through autoinoculation.

Dr. S. W. Becker: I agree with Dr. Wieder. Here is the reverse of the usual condition. There is usually normal skin with a few punched-out areas; in this case there are only remnants of normal skin, and most of the area shows noncontracting atrophic scarring. There may be a little keloid tendency in these ridges.

Dr. E. A. Oliver: I presented the case because the eruption was of a rather unusual type. I heartily agree with the diagnosis that has been made.

Leishmaniasis Americana. Presented by DR. TIBOR BENEDEK (by invitation).

S. A., a white man aged 26, was born in Chicago in 1912. When 2 years of age he went with his parents to Russian Poland. He stayed there for four years and returned to the United States in 1918. The family history is without interest. The patient is the second of five children; he has one brother and three sisters who are living and never have had any disease of the skin. The mother died of carcinoma ten years ago, but the father is living and well.

In the fall of 1933 the cartilaginous part of the nose, the alae and the septum nasi became red and swelled to about twice the normal size. The swelling gradually subsided, but about four weeks after the onset the nose began to become flat; the septum and the alae disappeared, and the nose collapsed. During this time there was a large amount of dirty discharge from the nose.

When the nose had almost totally collapsed he first sought medical care. At that time, on the basis of positive reactions to serologic tests, the diagnosis of congenital syphilis was made. Antisyphilitic treatment was started in the fall of 1934 and was continued more or less regularly until April 1937. The treatment, however, had no effect on the process in the nose. In April 1937, three and a half years after the nose collapsed, a small red papule appeared at the right commissure of the lips. This broke down, healed and broke down again two or three weeks later. In July this ulcer began to spread rapidly, and the patient entered the Cook County Hospital on September 17, the ulceration being at that time at the right commissure of the lips and the size of a half dollar. On the basis of positive serologic evidence the diagnosis of malignant syphilis was made. Antisyphilitic treatment had no effect; new lesions appeared, involving the entire upper lip.

On March 5 the patient came to the dermatologic department of the medical school of Northwestern University. At that time the right half of the lower lip and the left half of the upper lip were entirely destroyed, and the mucous surface of the remaining left portion of the lower lip showed a deep ulcus 20 mm. in diameter.

By means of histologic examination and cultural methods, syphilis, blastomycosis, sporotrichosis, tuberculosis and carcinoma were ruled out. Smears of material from the floor of the ulcer as well as the serous contents of a cantharides-induced blister showed typical leishmaniae. Sections made from two different parts of the ulceration showed the typical histologic structure of American leishmaniasis with massive proliferation of the epidermis and large infiltration of epithelioid cells and a few giant cells without tuberculoid structure. Leishmaniae were seen in histiocytes and free between the bundles of the edematous connective tissue in the corium. Sections and smears were submitted to Prof. Adolpho Lindenberg in Sao Paulo, Brazil, who confirmed the diagnosis. Recently (September 1938) the entire development of a single lesion was observed, and before the papule was broken down, hundreds of leishmaniae were recovered by puncture of the closed lesion.

At present the patient's face shows great destruction. The lower lip is entirely destroyed except for a 5 mm. stump at the right side, covered with an ulcer. Behind the left commissure of the lips, on the upper gum, there are flat ulcers with somewhat elevated and infiltrated borders from 5 to 10 mm. in diameter on the mucous surface. The skin shows several ulcers 15 to 20 mm. in diameter, above the left commissure of the lips, on the remainder of the philtrum nasi; the largest one is 30 to 35 mm. in diameter and is located on the right zygomaticus, with elevated, infiltrated edges and a dirty, granulating floor.

Repeated systemic examinations did not show any pathologic changes in the parenchymatous organs. Only the bone marrow of the right humerus showed in the roentgenogram a circumscribed area resembling osteomyelitis.

Throughout the course of this disease the patient has complained of "rheumatoid pains" in the muscles and bones, with swelling.

The red blood cell count and the hemoglobin concentration were normal; the white blood cell count dropped from 9,300 to 5,400; there were a decrease of the lymphocytes and an increase of mononuclear leukocytes.

From March 5 to July 14, 1938, the patient was given twenty-one injections of fuadin, and in August and September three treatments of 200 roentgens each. None of these treatments has been effective in checking the progress of the disease.

DISCUSSION

DR. MARCUS R. CARO: I disagree with the diagnosis presented. The patient's sister has been under my care for congenital syphilis. About four years ago the patient himself consulted me about a gumma of the nasal septum which resulted in the collapse of the nose. The gumma healed rapidly with antisyphilitic treatment, and the patient stopped coming in. He returned six months later with a large and destructive gumma of the upper lip. This also responded rapidly to treatment. The next time I saw the patient he was at the Cook County Hospital, where he was receiving antisyphilitic treatment for a lesion at the site of the present ulcer, which at that time had the clinical appearance of a gumma.

DR. M. H. EBERT: This man was in the hospital for several months. It was known that his sister was congenitally syphilitic and thought that he was. It was thought that he had a fulminating type of tertiary lesion of the face. The same history Dr. Caro described was obtained about similar lesions years before. Neoarsphenamine was given with iodides and mercury rubs. He responded not rapidly but fairly well, and after ten weeks he was apparently well. The lesion then began to break down again and did not respond as well to treatment. He left the Cook County Hospital. The condition was thought to be congenital syphilis. I was certainly surprised at Dr. Benedek's diagnosis.

DR. MARCUS R. CARO: Before accepting the diagnosis, one must consider the question of the transmission of leishmaniasis. As far as I know, this patient has not been away from Chicago for many years, and he has not been exposed to contact with the disease.

DR. TIBOR BENEDEK (by invitation): I should like to call special attention to this peculiar form of the Leishmania tropica var. braziliensis in smears under the microscope. The smear was made with the contents of a closed lesion of the upper lip. This observation is of great importance because all the Leishmania parasites found in this closed lesion were of this peculiar type, which has been described only twice in the whole international literature. Lanteri described this seemingly "budding" type of the Leishmania parasite as observed for the first time in a closed lesion in a case of oriental sore. This type of Leishmania has at first sight some slight similarity to a miniature yeast cell, but with proper staining it shows two distinct nuclei, the trophonucleus and the kinetonucleus. This observation, substantiating Lanteri's, makes it clear again that it is impossible to distinguish morphologically between the causative agent of oriental sore and that of the mucocutaneous form of the disease, leishmaniasis Americana.

Fixed Eruption (?) from Quinine. Presented by DR. THEODORE CORNBLEET and DR. J. B. ROBBINS (by invitation).

I., an Italian woman aged 39, has had an eruption on the hands, forearms and trunk for eight months. The lesions consist of macules which at times become edematous. It was found from the history and after administration of the drug that quinine produced an exacerbation in each of the lesions. Quinine was administered on three different occasions, and each time the lesions at the same sites became redder and puffy. On the third trial three or four new lesions appeared.

DISCUSSION

DR. JAMES H. MITCHELL: May I ask if phenolphthalein was also tested for? Some of the cold tablets contain that substance.

DR. OLIVER S. ORMSBY: Are there any cases of fixed eruption to quinine on record?

DR. THEODORE CORNBLEET: We did not test against phenolphthalein. Abramowitz has mentioned that fixed eruptions from quinine have been reported.

NOTE.—The week after the meeting the patient was given phenolphthalein; no lesions appeared.

Pigmented Nevi. Presented by DR. E. A. OLIVER and DR. W. W. TOBIN (by invitation).

D. P., an infant aged 8 months, has numerous brown pigmented patches scattered over the body, most of which, the mother states, were present at birth. However, since that time similar spots have continued to appear. There is no familial history of birthmarks. After an accidental cigaret burn of a pigmented spot above the left knee, the burned area lost its pigment.

The lesions vary in size from that of a matchhead to that of the palm. They are flat, chocolate brown and irregular. In addition there is a giant type of brown nevus on the upper part of the back and neck, which contains papillomatous nodules and a growth of coarse white hairs.

Lymphoblastoma. Presented by DR. M. H. EBERT and DR. A. SLEPYAN (by invitation).

W. T., a man aged 46, a mulatto, first noticed some scaling on the flexor surfaces of the arms in 1935. This scaling slowly extended to the trunk and lower extremities. At no time has it caused much discomfort, except a sensation of burning when he is warm. He perspires freely. About a year after the onset he noticed painless nodes.

The patient is apparently in good health. There is considerable ichthyosiform scaling on the covered portions of the body. The axillas are spared. The legs, waist, scapular areas and flexor surfaces of the arms are irregularly mottled with purplish red, poorly defined macules. The skin looks atrophic in these areas. Small areas of purpura are seen in the axillary folds and in the groins. The inguinal, femoral and axillary glands are enlarged to the size of a walnut and are movable and painless. There are a dime-sized, dull red raised plaque on the upper part of the back and some erosions about the waist.

The histologic sections presented are from a block imperfectly fixed and are unsatisfactory. Material for a second biopsy was taken from a slightly raised plaque on the lower part of the back.

There was some lamellated scaling, with occasional small areas of parakeratosis. In general the epidermis was thinned and the rete pegs flattened. There was migration of leukocytes through the epidermis in places. The upper third of the corium was edematous and was occupied by a fairly dense infiltrate made up of lymphoblasts, lymphocytes in various stages of evolution, reticulocytes and connective tissue cells. Several large cells showed mitotic division. There was a dense infiltrate about the vessels of the middle and lower portions of the corium as well as the hair follicles and the sweat glands.

The differential leukocyte count showed: lymphoblasts, 3 per cent; myelocytes, 2 per cent; young forms, 2 per cent; band forms, 3 per cent; segmented polymorphonuclear leukocytes, 48 per cent; eosinophils, 4 per cent; lymphocytes, 34 per cent, and monocytes, 3 per cent.

DISCUSSION

DR. OLIVER S. ORMSBY: The clinical characteristics in this case are those of what was formerly termed "idiopathic atrophy" of the skin. The point of interest to me is whether the blood picture and the conditions causing it are responsible for this particular kind of atrophy. One must recognize that a number of cutaneous lesions may occur in persons presenting apparent lymphoblastic blood changes. There may be no connection between the two. I have seen a patient with parapsoriasis who also had the blood picture of leukemia. Whether there was a causal connection between the two was never determined. Careful observation for a considerable period will be required to clarify this case.

DR. PAUL A. O'LEARY, Rochester, Minn.: The diagnosis of poikiloderma vasculare atrophicans seems justified; in fact, I believe there is a great similarity between this case and the case of poikiloderma presented by Dr. Perlstein. The cutaneous picture today called poikiloderma vasculare atrophicans impresses me as being the result of damage by various noxae to the cutaneous vascular structure. In fact, the damage may involve the structures deeper than the skin. Poikiloderma has been observed in association in one way or another with mycosis fungoides, disseminated lupus erythematosus and dermatomyositis, as well as with idiopathic atrophy. When poikiloderma follows disseminated lupus erythematosus or dermatomyositis, it may well be that the poikiloderma developed as a result of the damage caused by the same etiologic agent that produced the other diseases. Mycosis fungoides appearing in a patient with poikiloderma, or the reverse of this picture, likewise might well be due to common noxae. Accordingly, it would seem advisable to consider the cutaneous picture called poikiloderma as a development resulting from the influence of various agents, rather than as having a distinct etiologic factor.

DR. E. A. OLIVER: I agree with Dr. O'Leary. This picture is much like one I saw some years ago. The histologic sections were almost identical with the sections from that patient. I believe that his poikilodermic symptoms are simply part of the disease which is probably going to develop and which is probably mycosis fungoides. I might also add that that is a rather hazardous diagnosis to make, because mycosis fungoides is not at all common among Negroes; only 5 or 6 cases have been reported.

DR. OLIVER S. ORMSBY: This will perhaps add to the academic part of the discussion: The clinical manifestations of poikiloderma — the ones surely real poikiloderma—are patches of variable size, usually large, composed of pigmentation, telangiectasia and atrophy, and resemble healed radiodermatitis. There are no special sensations. The patches in the patient presented are merely atrophic; there may be some telangiectasia, but there is no pigmentation. I agree that poikiloderma-like symptoms occur secondary to or in association with a number of diseases. In this particular case idiopathic atrophy stands out prominently.

DR. RUBEN NOMLAND, Iowa City: I had the good fortune to study with Dr. Oliver (ARCH. DERMAT. & SYPH. **33**:*267* [Feb.] 1936) the case he mentioned. I believe that condition was a duplicate of this. There were widespread atrophy and decided infiltration of round cells beneath the epidermis. I believe this case is one of mycosis fungoides with poikiloderma-like lesions. The man I saw today had two or three infiltrated plaques that are going to be a part of mycosis fungoides.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Clinically as well as histologically I think this picture is fairly typical of acrodermatitis chronica atrophicans (idiopathic atrophy). The dense infiltrate is consistent with such a diagnosis, as are also the flattening of the rete ridges and a characteristic narrow strip of normal cutis between the infiltrate and the epidermis. Careful study of the cells under oil immersion lens failed to reveal any immature cells of the lymphocytic or myelogenous series. There was no clumping of cells to form pseudo giant cells, pyknosis or karyorrhexia such as one sees in mycosis fungoides. The histologic picture in this case is not that of poikiloderma. In the latter condition the histologic changes resemble those of lupus erythematosus, and there is definite liquefaction necrosis of the basal cell layer, a condition which does not exist in this case.

DR. M. H. EBERT: I am sorry that we were not able to study the case adequately. The patient is employed and is anxious to retain his position. If he enters the hospital, he will lose his position for the winter, so I think it best to let him go. The sections studied here were not satisfactory, and more will have to be made. I had little opportunity to study them, so I cannot talk well about the histologic changes.

Clinically the striking point is the ichthyotic scaling that involves all the covered portion of the body. The second point that strikes one in this study is the peculiar

purplish red discoloration of the skin. I realize how difficult it is to assay the value of change in color in the Negro race or in mixed races. There is extensive adenopathy of some duration. This may be due to drainage from the open areas on the skin, but I hardly think so. I think it is part of the pathologic process. In addition, there is tumor formation on the back. There are a great many arguments in favor of acrodermatitis, but it is my opinion that it belongs in the lymphoblastoma group. Some three or four years ago I presented a case of mycosis fungoides in a Negro. The man later died, and the diagnosis was verified by autopsy, so mycosis fungoides does occur in that race, although it is unusual. I should not say this is necessarily mycosis fungoides. There is a burning sensation in the skin when the patient is warm, but there is no real itching.

Dermatitis Factitia. Presented by Dr. David V. Omens and Dr. W. W. Tobin (by invitation).

I. S., a woman aged 42, single, states that ten years ago she had two boils on her face which were incised by her physician, who told her that she had "too much acid in her system." Since that time she has suffered from deep sores on the face, arms and legs. These began as red, itchy spots. She has applied only salves. She admits that scratching has a great deal to do with the formation of the sores, but the extreme nervous tension she is under at home makes it impossible for her to stop. The eruption has been worse for the past two months, but since the patient has been in the hospital the past five days the sores have improved, and no new ones have appeared.

Examination discloses sharply demarcated linear and oval clean ulcerations of the cheeks, neck, forearms, dorsa of the hands, legs and dorsa of the feet, which are intermingled with old atrophic scars.

General examination of the patient and serologic tests of the blood gave normal results.

DISCUSSION

Dr. Oliver S. Ormsby: I think the question should be clarified as to what is meant by the term "factitious dermatitis." A number of years ago all dermatitis produced by the patient was classed by Wilson as factitious. Later, when the patient admitted producing the lesions they were called neurotic excoriations. Certain lesions were described by Crocker under the title "acne keratosa." Colcott Fox used the term "dug-out excoriations" for the whole group. There is no doubt that some persons do injure their skin, sometimes seriously, in an effort to get relief from uncomfortable sensations or to remove some supposed foreign substance in the skin. I have seen excavations in the face large enough to hold a hazelnut and severe disfigurement produced by persons whose social position was high and in whom such disfigurement was of serious import. There existed in these patients an irresistible impulse to mutilate the skin. Such patients never resort to deception. All lesions so produced should be termed neurotic excoriations. In most cases of self-inflicted dermatitis the patient deliberately produces lesions but will not admit the fact. In a few a dual personality appears to be active, and the patient, though he produces the lesions, has no recollection of the circumstances. Both of these types of self-inflicted dermatitis should be classed as factitious and distinguished from neurotic excoriations.

Dr. James H. Mitchell: I agree with Dr. Ormsby. I have found that the patient has lesions in the scalp similar to those on the body. She admits she is impelled to get something out of the skin.

Dr. Paul A. O'Leary, Rochester, Minn.: For malingerers I have found that the use of pentobarbital sodium to the point of moderate inebriation frequently saves several days of effort in eliciting the basis for the feigned eruption. The drug is given with the purpose of releasing the patient's inhibitions, and when it is possible to produce a fair degree of intoxication, patients, particularly young women, are apt to talk freely.

DR. DAVID V. OMENS: This patient absolutely refused to admit that she produced these lesions herself, but I think she was subjected to a "third degree" every day or several times a day, with some one asking her about the lesions. It was only the last day or so that she finally admitted she was doing it.

DR. THEODORE ROTHMAN, Paterson, N. J.: In cases of factitial lesions I have found it useful to investigate the conjunctival and pharyngeal reflexes. If the patient has injured himself with caustics voluntarily, one finds usually a typical picture of hysteria with absence of reflexes. This aids in the differentiation of the condition from neurotic excoriations, which are usually not associated with hysteria.

Pityriasis Lichenoides et Varioliformis Acuta (Habermann). Presented by DR. MINNIE O. PERLSTEIN (by invitation).

L. M., a Jew aged 46, presents an eruption of six weeks' duration. He has previously been in excellent health; there has been no preceding disease of the skin. The eruption began with severe itching of the forearms, which was followed twenty-four hours later by generalized erythematous lesions involving the entire trunk from the neck to the knees. Twenty-four hours later the generalized erythema had somewhat subsided, and the patient presented a pityriasis rosealike eruption in the midaxillary areas and over the abdomen. This was associated with severe generalized itching. One week after the onset the lesions became vesicular, and later they were covered with an infiltrated black stuck-on crust. With the development of the severe inflammatory lesions there was associated a slight rise in temperature and general malaise. All the pityriasis rosea-like lesions underwent this cycle at varying times. When the crust fell, a varicella-like umbilicated scar remained. At the end of five weeks there was almost complete involution of the lesions.

Examination shows an eruption limited to the trunk, the greatest accentuations being in the midaxillary areas over the abdomen and in the flexural folds of the extremities. It consists of oval, salmon pink papulosquamous lesions, most of which have a varicella-like depressed center. In addition, there are scattered pustular lesions on an inflammatory base.

The secondary lesions consist of deep-seated inflammatory papules which vary in size from that of a matchhead to that of a hazelnut and are covered with a black crust.

Physical examination gives otherwise essentially negative results.

Examination of the blood disclosed the following values: hemoglobin, 91 per cent; red blood cells, 4,720,000; white blood cells, 8,100; neutrophils, 56 per cent; lymphocytes, 35 per cent; mononuclears, 5 per cent, and eosinophils, 4 per cent. On chemical examination of the blood the essential finding was a sugar content of 133.3 mg. per hundred cubic centimeters. Because of the acute manifestations of cachexia, biopsy was not performed.

DISCUSSION

DR. E. A. OLIVER: I think this case fits in well with the cases of Habermann's disease that have been heretofore presented and published. The only question in my mind concerns the peculiar pityriasis rosea-like distribution. During the past year I have observed a number of cases of pityriasis rosea that did not conform to the ordinary type. In this case one sees the typical distribution of pityriasis rosea but with the varicella-like eruption, hemorrhagic crusting and the type of lesion associated with pityriasis lichenoides et varioliformis acuta. I believe the condition is Habermann's disease.

Gold Dermatitis from Treatment of Leukoderma with Sodium Gold Thiosulfate. Presented by DR. E. A. OLIVER and DR. W. W. TOBIN.

E. M., a man aged 49, states that for three years he has had large white spots on his hands. Six months ago similar spots appeared on his neck. They have all appeared without any preceding inflammatory changes in the skin. He also states that for many years his mother has had a similar eruption on her hands.

He was given eight weekly injections of sodium gold thiosulfate, the dosage beginning with 25 mg. and increasing to 50 mg. He was told to expose the involved areas to sunlight as much as possible. After four injections the leukodermic patches seemed to be smaller. However, after the eighth injection the patient complained of a generalized eruption and intense itching. Examination disclosed a universal fine scaling erythematous dermatitis, which was more severe in the leukodermic patches.

At present, three weeks after the last injection of sodium gold thiosulfate, the dermatitis is greater than one week after the injection, despite repeated injections of sodium thiosulfate. The patches of leukoderma are approximately two-thirds the original size.

General examination of the patient before treatment disclosed nothing abnormal. The urine was not examined for hematoporphyrin. Serologic studies of the blood gave negative results.

DISCUSSION

DR. W. W. TOBIN: We presented this patient because he exhibits an interesting reaction to sodium gold thiosulfate, which was used in the treatment of his vitiligo. While he has generalized dermatitis, the more severe changes are limited to the vitiliginous areas. This would tend to indicate that sodium gold thiosulfate might be useful in the treatment of vitiligo, as Lindsay has pointed out.

A Case for Diagnosis (Bismuth Eruption?). Presented by DR. JAMES H. MITCHELL.

M. M., a woman aged 31, is a graduate nurse and hospital supervisor. She was first seen on March 16, 1938. At that time she had a primary lesion on the right side of the lower lip. The lesion had been present since the latter part of January and had not been recognized. There were generalized adenitis and a typical exanthem. The Wassermann reaction was strongly positive. The patient was given a series of twelve injections of 0.45 Gm. of neoarsphenamine, and on May 26 1 grain (0.06 Gm.) of bismuth subsalicylate in oil was given in the right buttock. At this time all symptoms had disappeared, and the patient was entirely free from any cutaneous changes.

She was next seen on June 9 by Dr. James Webster, who made a record that there were large lesions on the palms and flexor surfaces of the wrists, composed of erythematous plaques with a somewhat keratotic surface. She was given an injection of a bismuth preparation at that time, and this was repeated on June 15.

When she was next seen, on June 23, there were large psoriasiform lesions on the palms, with lesions scattered about the body elsewhere. There was intense itching, and a great deal of emotional disturbance was present because of the appearance of the lesions. She was given ½ skin unit (150 r) unfiltered, of roentgen rays on the palms and an injection of 0.45 Gm. of neoarsphenamine. The dose of neoarsphenamine was repeated on June 30 and on July 7, 14 and 21. By this time the lesions had entirely cleared, and the possibility of a recurrence of the lesions when injections of the bismuth preparation were resumed was discussed with the patient. She was given on July 28 1 grain (0.06 Gm.) of the bismuth preparation, and on August 5 there was a sharp recurrence on the palms and soles of the same type of psoriasiform lesion. She was then given a series of intravenous injections of sodium thiosulfate, but the lesions did not respond. Roentgen therapy was given on September 1, as well as more neoarsphenamine. A nodule formed at the site of the primary lesion on the right side of the lower lip. Rather extensive lesions are now present on the shins and various parts of the body. The needle puncture tends to produce a lesion at that point. The nails and scalp have remained free.

DISCUSSION

DR. JAMES H. MITCHELL: There are several points I did not make clear in the presence of the patient. In the first place the lesions on the palms would be

called squamous syphiloderms. I have never known a squamous syphiloderm to itch as these lesions do. The patient is under treatment with neoarsphenamine twice a week. This treatment has made no impression on the palmar lesions. That does not prove that the lesions are not squamous syphiloderms. The lesions elsewhere are not syphiloderms of any type known to me. The extreme itching, the disappearance of the lesions with the use of sodium thiosulfate and the recurrence with the use of the bismuth preparations make the case interesting.

DR. EDWARD A. SKOLNIK (by invitation): Although the cases I have reported were of a nonspecific type of dermatitis resembling pityriasis rosea, lichen planus and lichen simplex chronicus, I do not recall ever having seen a condition resembling this. I found that sodium thiosulfate will clear them up. I have known them to recur as many as three times, and each time they would clear up. Some of them are persistent, and I have had to treat them with sodium thiosulfate for as long as two months. It seems to me the lesions on the wrists are not those of bismuth dermatitis.

DR. OLIVER S. ORMSBY: I should like to ask Dr. Skolnik's opinion of the lesions on the trunk.

DR. EDWARD A. SKOLNIK: Those on the trunk could be a bismuth dermatitis because they are the type of maculosquamous lesions that I have seen.

DR. M. H. EBERT: One thing to be borne in mind is that if bismuth has been administered as bismuth in oil, a depot is formed which in some instances remains a long time. At the Cook County Hospital I observed a case that was rather puzzling. The lesions looked like persistent pityriasis rosea. I made a plate of the hips, and there were large deposits of bismuth remaining in the buttocks, although treatment had been stopped several weeks previously. In other words, a small amount of bismuth is left in the system when treatments are stopped. Later the persistent pityriasis rosea will disappear.

DR. H. R. FOERSTER, Milwaukee: It is worth while calling attention to eruptions resulting from bismuth, because they are uncommon. I recall a case in which the lesions were similar to those on the thigh of Dr. Mitchell's patient. The condition was a patchy eczematoid dermatitis that appeared in the absence of other cutaneous lesions during a course of bismuth therapy and resisted local treatment. The eruption cleared up shortly after discontinuance of the injections of the bismuth preparation and recurred later, when the injections were resumed. Presumably such eruptions are specific reactions to bismuth.

DR. EDWARD A. SKOLNIK: I definitely agree with Dr. Ebert as far as the depot of absorption is concerned. I have taken several roentgenograms of the site of injection as late as six months after treatment was discontinued and have found a shadow at the site of injection. That is probably the reason why some such eruptions do not respond readily to sodium thiosulfate.

DR. JAMES H. MITCHELL: It has been difficult to manage this patient because of her work as a graduate nurse and the necessity for secrecy. I think it would be advisable, as Dr. Ebert pointed out, to make some plates of the buttocks.

Healed Sporotrichosis. Presented by DR. DAVID V. OMENS.

J. W., a married man aged 43, a florist, was seen late in July and was referred to the Cook County Hospital with a diagnosis of tuberculous lymphangitis. Examination showed on the lateral aspect of the right arm about twenty abscesses, varying in size and occurring in linear formation, ending abruptly just above the elbow. This condition started with a single sore about a paronychia of the middle finger, and abscesses began to form about one month thereafter. This condition occurred during the gladiolus season.

The patient is suffering from tuberculous pleurisy, and aspiration is being done every three weeks. The pleurisy is on the left side and, because he may have scratched that area with his right hand, causing infection of the finger, a diagnosis of tuberculous lymphangitis was made elsewhere.

The Wassermann reaction of the blood was negative. A test for tularemia gave a negative result. Cultures and smears for sporothrix were positive. Treatment consisted of placebo roentgen therapy (37 r every two weeks for five treatments).

DISCUSSION

DR. H. R. FOERSTER, Milwaukee: Of interest in this case is the definite effect following small doses of roentgen therapy. Sporotrichotic lesions are usually radiosensitive, and I believe the several roentgen exposures produced sufficient reaction through cumulative doses to result in involution of the lesions, though the disease may be merely latent.

DR. DAVID V. OMENS: I gave roentgen treatment for its placebo effect. I did not realize that sporotrichosis is as radiosensitive as it proved to be in this case. After the first treatment it improved 50 per cent.

MANHATTAN DERMATOLOGIC SOCIETY

MAX SCHEER, M.D., *President*

Oct. 11, 1938

ANTHONY C. CIPOLLARO, M.D., *Secretary*

A Case for Diagnosis (Parapsoriasis? Mycosis Fungoides?). Presented by DR. FRED WISE.

S. L., a man aged 28, a patient of Dr. Charles Rein, was first examined on Sept. 21, 1938. He had an eruption of thirteen years' duration. In 1912 he suffered from an attack of anterior poliomyelitis, which has left him with a residual deformity of the left foot.

The eruption affects chiefly the lower part of the abdomen, the buttocks, the thighs and the feet. On the trunk and thighs there are numerous discrete and confluent scaly plaques, somewhat elevated, dusky red and moderately infiltrated. On the anterior surfaces of the thighs the lesions show a tendency toward stripe formation, and a somewhat reticulated appearance is caused by islands of unaffected skin lying mosaic-like within actively inflamed plaques. The interdigital areas of the toes show a considerable amount of scaling and maceration, and the lateral surfaces of the feet are inflamed and hyperkeratotic. The patient complains of intense itching. Only temporary improvement has resulted from roentgen ray treatment, injections of solution of posterior pituitary and many topical applications.

DISCUSSION

DR. PAUL E. BECHET: Serious consideration should be given to the possibility of mycosis fungoides in this case. While I admit that the lesions are characteristic of parapsoriasis en plaques, it is known that mycosis fungoides frequently simulates both psoriasis and parapsoriasis for a long time before demonstrating the changes characteristic of mycosis fungoides. The patient has a few infiltrated circinate plaques which, he claims, itch, but there are no scratch marks. In view of the infiltration and the circinate arrangement of many of the plaques, I think that the eruption belongs to the mycosis fungoides group.

DR. DAVID L. SATENSTEIN: This case is somewhat similar to the one that Dr. Fraser presented before this society with a clinical diagnosis of psoriasis. A year later, according to the report he gave at that time, the patient presented the clinical picture of mycosis fungoides. Death occurred later. I believe that in all cases in which there are large plaques persisting for any length of time

and in which the clinical question of psoriasis or parapsoriasis comes up, one must consider the possibility of mycosis fungoides or any one of the reticulo-endothelial processes. This picture develops gradually, and it is a long time before one is able to establish the microscopic diagnosis. I believe that the errors made in such cases are not errors on the part of the clinician but are due to the pathologist's lack of study of the slides.

DR. ISADORE ROSEN: This is one of those unusual cases in which a definite clinical diagnosis cannot be established without the aid of the microscope. Certain features suggest both psoriasis and parapsoriasis. I have seen this combination in certain patients. As the lesions in this case have been present about fifteen years without any clinical evidence of mycosis fungoides and as there are areas on both feet which resemble psoriasis, I am inclined to favor a diagnosis of psoriasis rather than one of parapsoriasis.

DR. E. WILLIAM ABRAMOWITZ: One ought to consider that the eruption has been somewhat modified by treatment. The patient may have arsenical keratoderma in addition to psoriasis of the soles, but I am more inclined to the diagnosis of mycosis fungoides.

A Case for Diagnosis (Dermatitis Herpetiformis?). Presented by DR. MAX SCHEER.

D. G., a woman aged 47, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 8, 1938, with an eruption in the mouth and on the chest and back of four weeks' duration.

On September 11 the patient had an itching eruption which began in the midline of the lower part of the back. Spots appeared, followed by intense itching. These spots soon became blisters. To avoid scratching, the patient rubbed with her clothing for relief. The blisters broke and exuded a clear fluid which had a decidedly "queer" odor. The blisters soon dried, leaving a crust. On October 1 a similar outbreak occurred on the middle of the chest and also on the breasts. Since then more lesions have appeared, spreading all over the abdomen. About a week ago the patient felt a stinging sensation in the mouth, at the base of the tongue anteriorly. A blister appeared and ruptured, leaving a raw, red area which is still sore. Another vesicle appeared on the upper gingival margin of the right lower jaw posteriorly. At about the same time the patient noticed a scratchy sensation and soreness in the throat on swallowing.

The patient does not feel ill and says her health has been good for years. She does, however, feel worried about the present eruption, which she believes is becoming worse. She has had measles and chickenpox. The menses are regular as a rule, but of late they are accompanied with pain in the back. There are no gastrointestinal symptoms. The bowel movements are regular. She claims to have taken no medication for twenty-five years. She does not have headaches. Her teeth are in poor condition. The Nikolsky sign is negative.

NOTE.—Two days after presentation the patient returned to the clinic, complaining of increased itching. She now showed a profuse outbreak of grouped vesicles on the back. The clinical picture was characteristic of Duhring's disease.

Lichen Planus, Involving the Scalp. Presented by DR. ISADORE ROSEN.

F. M., a man aged 53, presented himself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in September 1938, with an eruption on the scalp of one year's duration.

The entire scalp is uniformly involved by an erythematous, violaceous eruption, atrophic in certain areas. There is also marked alopecia. On the cheeks and the posterior portion of the neck are isolated erythematous, violaceous and atrophic lesions which strongly suggest lichen planus. On the trunk, covering the entire back down to the coccyx, are isolated lesions typical of lichen planus (not of the atrophic type), while on the chest numerous isolated atrophic lesions are present.

The histologic picture of lesions from the scalp and the trunk was that of typical lichen planus. The blood picture was normal. The Wassermann reaction was negative.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: The patient had definite pustules on the scalp, and atrophy. Without the lesions on the body I should not have given a second thought to any other diagnosis than folliculitis decalvans. In fact, when the first biopsy was reported I did not accept the diagnosis of lichen planus of the scalp, because I know that on occasion the picture reported by the pathologist as typical of lichen planus will prove to be something else after further observation. The clinical appearance of the lesions on the scalp has changed. There are few pustules. There is a question whether this patient has secondary folliculitis.

DR. DAVID L. SATENSTEIN: Microscopic examination revealed lichen planus of a lesion on the body, and one of the pieces of tissue from the scalp showed a similar structure.

DR. E. WILLIAM ABRAMOWITZ: I believe the patient also had lesions on the lips, and lupus erythematosus was also considered.

DR. ISADORE ROSEN: I agree with the remarks made by Dr. Abramowitz. If the lesions on the scalp are lichen planus, it is the first case I have ever observed in which there was such extensive involvement.

Toxic Eruption of Pregnancy. Presented by DR. MAURICE COSTELLO.

M. S., a married woman aged 25, eight months pregnant, has had a severely excoriated papular eruption on the extensor surfaces of the extremities and the upper part of the back and the abdomen for the past two weeks.

DISCUSSION

DR. PAUL E. BECHET: I think this condition belongs to the group of papular or vesicular and bullous eruptions described many years ago by Bulkley under the title of herpes gestationis. The lesions were not always grouped. They were isolated and discrete, on the arms and legs. This type of eruption invariably undergoes involution within a reasonably brief period after pregnancy. It is undoubtedly a toxic manifestation of pregnancy and cannot be differentiated from dermatitis herpetiformis.

DR. MAX SCHEER: One occasionally encounters pruritus which appears in and persists throughout pregnancy and which disappears after childbirth. Such pruritus is unaccompanied by lesions (except scratch marks). In my opinion it is not to be put in the category of herpes gestationis, which produces cutaneous lesions and is a rare disease.

DR. DAVID L. SATENSTEIN: If I had seen these lesions in a young person, I should possibly have called it a mild form of toxic prurigo.

DR. E. WILLIAM ABRAMOWITZ: Irrespective of their morphologic character, these eruptions are looked on as resulting from an endocrine rather than a toxic disturbance, and investigation from the endocrine aspect may be of practical benefit to the patient. It has been observed that such eruptions are more apt to appear when a male child is being carried.

DR. GEORGE M. LEWIS: It is probably not an upset in the mother's endocrine system that is responsible for this condition. A rational explanation is that the mother's skin became sensitized to certain hormones which are normally produced during the last few months of pregnancy.

DR. MIHRAN B. PAROUNAGIAN: I see no reason why this disease should be called by any other name than herpes gestationis. The condition, it is known, occurs during pregnancy. It is an extremely pruritic herpetic eruption and disappears at the conclusion of pregnancy.

DR. E. WILLIAM ABRAMOWITZ: Etymologically the word "herpes" means to creep.

DR. MAX SCHEER: Today the term herpes is applied to certain diseases with vesicular lesions, although that was not the original meaning. I think that Dr. Costello's view that this is a toxic eruption is absolutely correct. The cause is not known. I do not see why it should be called herpes when there is not any herpes. One might call it pruritus of pregnancy (pruritus gestationis).

DR. MAURICE COSTELLO: About 4 per cent of the 1,500 pregnant women delivered at Misericordia Hospital, New York, yearly present this eruption. In every instance the eruption is similar in location, appearance and time of occurrence. It begins in the latter months of pregnancy and disappears within a week after delivery. Vesicles and bullae are never seen in association with this eruption, which differentiates it from herpes gestationis. It is probably of endocrine origin.

A Case for Diagnosis (Dermatolysis? Macular Atrophy?). Presented by DR. FRED WISE.

J. F., a woman aged 37, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 4, 1938.

She presented an eruption of two years' duration on the anterior aspect of the right shoulder. It extended down the outer aspect of the arm to within 6 cm. of the elbow joint. The lesion was roughly rectangular, approximately 15 cm. in length and 6 cm. in width. The surface was somewhat lighter in color than the unaffected skin surrounding it, and the consistency was soft and flaccid, somewhat resembling a layer of uncongealed gelatin. With the light striking the area at an angle, a slight elevation of the plaque was discernible. During the past six months a new lesion, discoid and about 2 cm. in diameter, appeared about 10 cm. below the original plaque. Two months ago a dime-sized area, very faint in outline, appeared on the forearm. Subjective symptoms have been absent. Histologic examination showed a process reported as "resembling von Recklinghausen's disease."

DISCUSSION

DR. DAVID L. SATENSTEIN: The specimen was originally sent to the laboratory with a diagnosis of lymphectasia. Two pieces of tissue were sent in, and I observed a definite, circumscribed cellular mass suggesting some form of neoplasm, the type of which I could not decide on, because not enough work was done on it. No diagnosis was established. I saw the section yesterday afternoon, and I would not make a diagnosis from it. My associates and I did exclude the possibility of its having to do with lymphatics. There was nothing in the specimen that suggested any form of malignant neoplasm. Clinically I got the impression that it was a boggy or doughly tissue, and I am under the impression that some type of degeneration is present, but what it is I do not know. The changes suggesting it had nothing to do with the fat. They were in the cutis, and the fat was not changed.

NOTE.—The final microscopic diagnosis was von Recklinghausen's tumor.

Dermatitis Lichenoides Chronica Atrophicans. Presented by DR. FRED WISE.

M. B., a woman aged 51, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, on Sept. 15, 1938.

She has a cutaneous disease of eight years' duration, which involves the front and sides of the neck, shoulders, chest, back, abdomen, arms and forearms (up to the wrists) and the skin overlying the shins. On the neck, chest and upper portion of the back the skin is tense, waxy white, smooth, glistening and devoid of surface markings. Clinically these changes are indistinguishable from those of diffuse scleroderma in the stage of tense atrophy. On the flexor surfaces of the upper extremities the lesions present closely crowded hard elevated papular elements with a rosy red tint, forming large plaques with well defined borders,

surrounded in part by a violaceous zone. On the anterior surface of the legs the process resembles the atrophic stage of scleroderma. Isolated morphea-like plaques are present on the abdomen and on the lower aspect of the back.

Histologic examination showed the end stages of an atrophying process. There was pronounced edema throughout the cutis; in the upper and the middle portion the vessels and lymph spaces were dilated. There was a moderate perivascular infiltrate composed mostly of small round cells. The elastic tissue was stretched and fragmented. The epidermis was thin and flattened.

DISCUSSION

DR. DAVID BLOOM: I am glad to observe this case and to be able to compare it with the case of lichen atrophicus et sclerosus which I presented last year (ARCH. DERMAT. & SYPH. **35**:1200 [June]; **36**:880 [Oct.], and **36**:1115 [Nov.] 1937). In that case the papules were first violaceous and shiny, indistinguishable from the papules of lichen planus. They were arranged mostly in the form of round plaques, the centers of which presented roughening produced by follicular spines. The histologic picture of Hallopeau's disease is also different from that of Csillag's disease.

Sarcoidosis. Presented by DR. MAX SCHEER.

E. H., a woman aged 24, married, born in the United States, is presented from the outpatient department of the Mount Sinai Hospital.

She has an eruption of six months' duration on the chest, the back, the upper parts of the arms, the sides of the neck and the cheeks. There are about three dozen discrete lenticular papules and nodules, varying in size from that of a match head to that of a bean. The smaller lesions are yellowish pink and the larger ones reddish brown. There is fine telangiectasis over and around some of them. Diascopic examination shows them to range in color from yellow to brown. The patient also presents verrucae on the hands, of two years' duration.

The patient was treated in 1928 in the hospital and in the outpatient department for diabetes mellitus, abscess of the thigh and diabetic coma. She has been observed for the last ten years. About one year ago she had a cough; she had frequent colds, enlarged lymph nodes and occasional elevation of temperature. She was admitted to the hospital on Feb. 21, 1938, and discharged back to the outpatient department on March 5. The spleen and liver were found to be enlarged. The axillary and inguinal lymph nodes were removed for microscopic study. The histologic report on an inguinal node (February 27) was as follows: "epithelioid cell tuberculosis of the lymph node; no tuberculosis observed." The histologic report on an axillary lymph node (March 1) was the same.

Roentgen examination of the bones of the hands and feet was reported (March 1) as showing no abnormality. A guinea pig was inoculated with the biopsy material but died before the test period was concluded.

When the patient was discharged to the outpatient department on March 5, the diagnosis made was "Boeck sarcoid (lymph nodes and spleen)."

The eruption appeared about the middle of April and was first observed in the clinic for thoracic diseases.

The Wassermann reaction was negative. Urinalysis revealed no sugar but did reveal a trace of albumin. Examination of the sputum for tubercle bacilli on several occasions gave negative results. Several roentgenograms were made of the chest, the last report (Sept. 14) being "diffuse, very fine miliary infiltration of both lungs with enlargement of the paratracheal glands. The process is presumably tuberculous."

Dr. Samuel Peck made the microscopic examination and reported the tissue to be "sarcoid with an unusually large number of giant cells."

Graded tuberculin tests gave negative reactions.

Necrobiosis Lipoidica Diabeticorum. Presented by Dr. Fred Wise.

B. P., a woman aged 33, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept. 8, 1938.

The patient presents an eruption of three years' duration which consists of lesions on the anterior surfaces of both legs, the abdomen and the left submammary region. These are sharply defined, irregularly outlined, dark yellow and ivory-tinted, somewhat depressed and considerably indurated plaques approximately 4 to 5 cm. in diameter. On the right shin there are three individual plaques, and there are two similar lesions on the left shin. A faintly violaceous zone surrounds some of these lesions, and the surfaces show telangiectatic vessels.

The urine gave a 4 plus reaction for sugar. Chemical examination of the blood showed the following values: total cholesterol, 235 mg.; cholesterol esters, 60 mg., and lecithin, 260 mg., per hundred cubic centimeters of whole blood. The Wassermann and Kahn reactions were negative.

DISCUSSION

Dr. David L. Satenstein: There is nothing to say about the clinical side of this case, because it is as fairly characteristic as any I have ever observed, but something can be said about the pathologic changes. I believe, so far as the disease is basically vascular, with necrosis and fatty changes in the surrounding tissues, that the patients are likely to have further vascular disease, possibly diabetic gangrene. I have 1 such case under observation at present.

Papulonecrotic Tuberculid of Unusual Distribution. Presented by Dr. Maurice Costello.

N. L., a married woman aged 42, has had discrete papulopustular crusted lesions on the extensor surfaces of the elbows and knees and on the suboccipital and inframammary regions since April. She had similar lesions in 1932, 1933, 1935 and 1936, beginning in the spring. Interspersed with the present active lesions are many punched-out oval pea-sized white cicatrices. The lesions in the suboccipital and inframammary regions are more superficial. A roentgenogram of the lungs showed no evidence of tuberculosis, and the Wassermann reaction of the blood was negative. The case is presented, first, because of the unusual locations involved and, secondly, because of the prompt response to therapy. The patient was given two 0.3 Gm. doses of neoarsphenamine at weekly intervals.

DISCUSSION

Dr. David L. Satenstein: I should like to disagree with the diagnosis and call this condition ordinary pyoderma. The location is rather unusual for papulonecrotic tuberculid, and the scars do not have the usual depressed or punched-out centers.

Dr. E. William Abramowitz: It is known that the arsphenamines may be effective in treatment of papulonecrotic tuberculid. The old healed scars over the left scapula remind one of old syphilitic lesions, but the other lesions do not look like syphilis. Nevertheless, I think that that condition should be more definitely excluded.

(All others present agreed with the diagnosis of papulonecrotic tuberculid.)

Keratoderma Palmare et Plantare (Noncongenital). Presented by Dr. Fred Wise.

A. F., a man aged 28, an Italian, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on July 14, 1938. During the past three years he has noticed that his palms and soles have become thickened, dry and hard. In the past year the dryness has extended to the lateral surfaces of the feet and hands and to the dorsal surfaces of the fingers. More recently the skin of the elbows and knees has become involved in the same process.

During the past six months the condition has been growing progressively more pronounced in all areas. The patient does manual labor as a longshoreman. He is not aware of ever having taken arsenic or of having handled the drug in his work at various jobs.

The palmar and plantar surfaces are hard, dry and hyperkeratotic; the lateral and parts of the dorsal surfaces of the hands and feet are similarly affected. The extensor surfaces of the upper and lower extremities present elongated areas of pronounced hyperkeratosis, the affected regions being dusky red. The outline of the hyperkeratotic areas on the extremities is triangular, the knees and elbows forming the base of the triangles. The nails are unaffected. The diagnosis of mal de Meleda has been entertained. The Wassermann reaction of the blood is negative. The histologic report indicates advanced hyperkeratosis.

DISCUSSION

DR. PAUL E. BECHET: It seems to me that all of the various manifestations represent a single dermatosis, and I strongly suspect that erythroderma ichthyosiforme is the correct diagnosis despite the fact that the patient is 28 years old and the eruption did not manifest itself before the age of 24. The dermatosis in question presents many anomalies, and it is possible that it may make its first appearance some years after birth; then again, one cannot rely definitely on the patient's statement of the duration of his dermatosis. I should not consider the diagnosis of arsenical keratosis.

DR. DAVID L. SATENSTEIN: The patient has been working with metals, and on that basis I suggest the possibility of dermatitis due to some heavy metal. I think that the condition might be caused by contact, but it is probably due to inhalation of metals.

DR. LUDWIG OULMANN: I cannot agree with the diagnosis. I consider this an inflammatory process with peeling, which extends to the dorsal surfaces of the feet. The neurodermatitis-like patches on the extensor sides of the forearms are a part of the process. I have seen psoriasis develop in patients with such lesions.

DR. DAVID BLOOM: The association of palmar and plantar hyperkeratosis with extension to the backs of the hands and feet and also with ichthyosiform lesions on the knees, elbows and elsewhere resembles the clinical picture of so-called mal de Meleda. This case is an example of the acquired form. The changes I have seen produced by inorganic arsenic were papular keratoses on the palms and soles and not diffuse keratoderma as in this case.

DR. E. WILLIAM ABRAMOWITZ: I cannot accept a diagnosis of arsenical keratoderma. There are two types of keratoderma caused by arsenic, whether inorganic, organic, trivalent or pentavalent. The inorganic compounds are more apt to produce isolated or discrete keratoses of the palms and soles. The lesions appear a long time after the arsenic has been taken. Keratoderma developing immediately is from both the organic and the inorganic compounds. Both types were described as occurring in the Manchester (England) epidemic—with other symptoms of arsenical intoxication. If the patient handled an arsenical compound it simply was an added factor in bringing out an inherent tendency toward palmar keratoderma.

Xanthoma Tuberosum Multiplex. Presented by DR. MAURICE COSTELLO.

P. M., a man aged 31, a Filipino, has had an eruption for eight years. It consists of discrete and coalescing pea-sized to palm-sized golden yellow smooth areas which show a tendency to nodule formation on the elbows and knees. Yellow linear lesions following the normal creases of the palms are an interesting feature of this case.

The cholesterol content of the blood was 370 mg.; the nonprotein nitrogen content, 36 mg.; the creatinine content, 1.3 mg.; the sugar content, 105 mg.; the

calcium content, 11.3 mg, and the phosphorus content, 3.9 mg., per hundred cubic centimeters. The Wassermann reaction was negative. The erythrocyte count and the hemoglobin content were normal. There were 4,900 leukocytes per cubic millimeter of blood, with 75 per cent of polymorphonuclear leukocytes and 25 per cent of lymphocytes.

Amyloidosis Cutis. Presented by Dr. E. William Abramowitz.

J. O., a man aged 61, was first seen on Aug. 29, 1938, at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with an eruption on the legs of ten years' duration.

The patient has profuse follicular and papular lesions on the shins, extending to the calf. The papules are yellow-brown and firm to the touch. There is some itching. In the axillary areas are brownish, pigmented macular lesions of tinea versicolor. The general health is good. The histologic picture showed amyloidosis cutis. The patient is receiving roentgen therapy to the affected areas.

DISCUSSION

Dr. David L. Satenstein: I had 1 patient with this condition, and I got a reaction with an injection of congo red. I told the woman that it was practically hopeless but that we would try to do something. Treatment was started with 1 per cent crude coal tar, the concentration gradually being increased until full strength tar was given. A reaction set in, and when this reaction subsided the lesions had apparently disappeared. I do not know whether the lesions reappeared or not, but the last time I saw her the condition was practically all gone.

Senear Usher Syndrome. Presented by Dr. Maurice Costello.

L. F., a Negro aged 41, has had a vesiculobullous eruption on the left cheek covering an area about the size of a silver dollar for the past two years. The bullae are usually preceded by erythema accompanied by itching and burning. He had a similar eruption on the left cheek, which disappeared spontaneously, leaving pigmentation and slight atrophy. He also has many grayish white, oval and linear, flat and slightly elevated lesions on the buccal mucosa and the palate. He was not aware of the presence of the oral lesions. He received twenty roentgen ray treatments elsewhere, without therapeutic effect.

DISCUSSION

Dr. Fred Wise: I suggest the diagnosis of lupus erythematosus pemphigoides. Some of the lesions are almost identical in appearance with those of a patient that I had presented several years ago.

Dr. Max Scheer: A patient with exactly similar lesions was observed at the Mount Sinai Hospital some years ago. Dr. Wise diagnosed the eruption as bullous lupus erythematosus. The lesions resisted all therapy except treatment with a gold compound.

Dr. E. William Abramowitz: There is an increase in lupus erythematosus in this city, not only in white persons but also in Negroes. If the lesions do not respond to conventional therapy, I suggest a trial of sulfanilamide.

Extensive Blastomycosis of the Face, Neck and Torso. Presented by Dr. Fred Wise.

A. A., a man aged 45, an Italian, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on July 7, 1938. An eruption, which he stated was contracted in West Virginia, first appeared twelve years ago. The disease involved the larger part of the right side of the face, the entire circumference of the neck and the upper portions of the chest and back. Active elevated crusted and hyperkeratotic lesions affected the face, causing severe ectropion, from scar contraction, of the right lower eyelid and distortion

of the lips. On the right side of the neck a uniform area of contractile scar tissue developed, concealing the outline of the jaw and extending down over the clavicle to the midarea of the chest. The scar tissue caused immobilization of the head. Active cauliflower-like elevated lesions from 1 to 4 cm. in diameter appeared within the scar tissue of the chest and back. A larger area of the back of the neck became the seat of a shallow, sluggish ulcer with sharp margins and a granulomatous surface. During hospitalization the lesions have improved greatly with roentgen ray therapy and the administration of potassium iodide. Microscopic observations confirmed the diagnosis.

DISCUSSION

DR. MAX SCHEER: I saw this patient when he first came to the clinic, and there is a striking improvement.

DR. LUDWIG OULMANN: This case reminds me of one which I presented here twenty-five years ago. The case is illustrated in a textbook by Sutton. My patient improved in the beginning but contracted blastomycetic pneumonia, from which he died.

Trichorrhexis Nodosa. Presented by DR. FRED WISE.

S. S., a man aged 58, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on July 20, 1938, complaining of progressive diffuse loss of hair and constant itching of the scalp for the past two years. He is obviously of a nervous temperament and has the habit of frequently rubbing his head with his hands. He has a closely cropped tonsure; the hair is coarse and appears to be somewhat matted. There is a moderate inflammatory reaction of the scalp. Microscopic examination of the hairs showed the typical fracturing and node formation of trichorrhexis nodosa.

Lichen Nitidus—Unusually Extensive Involvement of the Palms. Presented by DR. PAUL E. BECHET.

Papulonecrotic Tuberculid. Presented by DR. PAUL E. BECHET.

Neurodermatitis Simulating Lichen Planus Hypertrophicus. Presented by DR. PAUL E. BECHET.

Lichen Planus. Presented by DR. ISADORE ROSEN.

Buccal Lupus Erythematosus or Lichen Planus? Presented by DR. FRED WISE.

MAX SCHEER, M.D., *President*

Nov. 9, 1938

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Naevus Comedonicus. Presented by DR. MAX SCHEER.

H. K., a boy aged 8 years, a ward of the Hebrew Orphan Asylum, has had a lesion on the left side of the neck since birth. The clinical features are typical of naevus comedonicus. In a linear area on the left side of the neck, about 3 inches (7.5 cm.) long and ¾ inch (1.8 cm.) wide are numerous comedos. There are also several round and oval atrophic areas about ½ inch (1.3 cm.) in diameter. Removal of the comedos was followed by their reappearance in the same locations in a few days.

No treatment has been given. The patient is presented for suggestions as to therapy.

DISCUSSION

DR. FRED WISE: I advise that the lesion be left untreated, or, if the guardians insist on its removal, that ablation be done, followed by skin grafting.

DR. ANTHONY C. CIPOLLARO: I agree with what Dr. Wise has said. However, if the lesion must be removed I should consider destroying it by electrodesiccation with the region under local anesthesia.

DR. ANDREW J. GILMOUR: I think this might be treated by electrolysis. If that does not succeed, more radical treatment should be used.

DR. DAVID L. SATENSTEIN: If the lesion is superficial the curet will give the best results.

DR. LUDWIG OULMANN: My treatment in such cases consists of superficial electrocoagulation followed by scraping with a sharp curet.

DR. MAX SCHEER: My opinion is that it should be either left alone or excised. I think it is a good area for excision, and I feel sure the result would be good.

Epidermodysplasia Verruciformis (Lewandowsky and Lutz). Presented by DR. FRED WISE.

M. T., a single man aged 23, born in the United States of Italian parentage, states that "warty" lesions first appeared on his hands and forearms at the age of 5 years. He was examined by me at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for the first time a few days previous to presentation but has been under the observation of other dermatologists for several years and has received a series of roentgen treatments for "multiple warts."

The eruption involves the face, scalp, palms, backs of the hands, forearms, legs and dorsa of the feet. The lesions on the face simulate verrucae planae; they are closely sown on the forehead and cheeks, vary in size from 2 to 4 mm. in diameter and are round and oval, flat topped, yellowish brown, slightly scaly and of the consistency of normal skin. On the forearms, hands and wrists the individual lesions are darker, more elevated and more scaly and show a tendency toward confluence. On the anterior aspects of both legs and on the feet the papular elements range from several millimeters to 2 cm. in diameter. They occur in the form of isolated as well as fused rounded, octagonal and oval lesions, many of them scaly and lichenified. On the anterior surfaces of both wrists are groups of papular lesions which closely simulate those of lichen planus. These lesions have been present for many years and exhibit no tendency toward regression. The palmar lesions are more indurated and lichenified than those on other parts of the body. The patient complains of mild itching. Physical examination shows no abnormalities aside from the eruption.

In addition to the generalized eruption there are several common warts on the hands and beneath several finger nails.

This example of the disease described first by F. Lewandowsky and W. Lutz (*Arch. f. Dermat. u. Syph.* **141**:193, 1922) appears to be the first reported in the United States.

DISCUSSION

DR. DAVID L. SATENSTEIN: A good many of the lesions look like warts clinically and histologically, but they are not warts.

As this condition has been present for many years without any change, I do not see how psychotherapy could have any effect. I should leave it alone unless infection occurs and should then destroy it.

DR. DAVID BLOOM: While common warts can easily be destroyed by electrodesiccation, verrucous nevi are much more difficult to treat. I should like to ask Dr. Wise whether the lesions of this patient, which resemble verrucae planae, are less responsive to treatment than are flat warts.

Neurotic Excoriations. Presented by DR. GEORGE M. LEWIS.

J. K., a man aged 26, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He states that he has noticed loss of hair for the past four years. He admits self traumatization.

Examination reveals three areas of alopecia on the scalp, somewhat irregular in outline. The skin in the patches is sclerotic. There is one crusted lesion. There is no evidence of seborrheic eczema, tinea capitis (favus) or staphylococcic folliculitis.

DISCUSSION

DR. ISADORE ROSEN: To one looking at this condition without knowing anything of the history, the presence of atrophy with pustular lesions suggests folliculitis decalvans. It would be impossible to produce such a clinical picture by pulling out hairs.

DR. MAURICE COSTELLO: The history states that this boy has been seen picking and scratching his scalp and that this has resulted in deep excoriations. The destruction of tissue and the resulting cicatrices have caused small areas of alopecia. I believe that the condition he now presents is the result of deep neurotic excoriations.

DR. MAX SCHEER: Scarring and atrophy can be present in other conditions when the skin is traumatized. From the history it appears to me that the scarring and folliculitis are traumatic in this case.

DR. ANTHONY C. CIPOLLARO: I saw this patient for the first time tonight. Dr. Lewis saw him at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, where he has been under observation and study. Dr. Lewis found no evidence of folliculitis decalvans, lupus erythematosus or other conditions that produce alopecia. Because of the definite history that this patient digs and rubs these areas, the diagnosis of dermatothlasia was made.

Naevus Verrucosus Linearis of the Palm. Presented by DR. FRED WISE.

A. P., a girl aged 8 years, presents a verrucous linear lesion on the left palm at the base of the middle, ring and little fingers and the corresponding interdigital spaces. The lesion is approximately 1½ inches (3.7 cm.) long and ¼ inch (0.6 cm.) broad and consists of firm, elevated, closely agminated verrucous formations which adhere firmly to the underlying skin. The mother first noticed it when the child was 2 years old.

The patient is presented for consultation as to the best method of treatment.

DISCUSSION

DR. DAVID L. SATENSTEIN: I saw a patient with a similar lesion on the sole, along the base of the toes, and I obtained a good result by cleansing the area with carbon tetrachloride to get rid of the grease and then swabbing the lesion with full strength solution of formaldehyde. This is to be repeated every few days.

DR. ANTHONY C. CIPOLLARO: I should treat this lesion by electrodesiccation and curettage after local anesthesia with procaine hydrochloride. Often the scar that follows electrosurgical measures is soft and pliable. Of course, keloids occasionally form.

DR. DAVID L. SATENSTEIN: I have treated many such lesions by electrodesiccation, especially when found on the palms and soles, but I found that it took six to eight weeks for them to heal. I should not accept that as the method of choice.

DR. E. WILLIAM ABRAMOWITZ: I should suggest the preliminary use of a 40 per cent salicylic acid plaster to clear up some of the hyperkeratosis, and follow it with application of solid carbon dioxide.

DR. MAX SCHEER: I observed a case of lesions exactly like these except on the neck. The patient was a ward of the Hebrew Asylum, and Dr. D. Ballin obtained

an excellent cosmetic result. The treatment was given every two or three weeks. Solid carbon dioxide was used, with firm pressure for one or two minutes, and the result was good.

DR. FRED WISE: I should be inclined to try nonsurgical treatment, because in my experience electrodesiccation and curettage in cases of nevoid warts or nevoid formations associated with hyperkeratosis usually has been unsuccessful. Sometimes the scar was worse than the original condition.

Lupus Erythematosus Precipitated by Sunlight After Sulfanilamide Therapy. Presented by DR. MAURICE COSTELLO.

E. A., a woman aged 37, has had an eruption for six weeks. She states that on June 18 she was given sulfanilamide tablets for a vaginal discharge. She was instructed to take two 5 grain (0.32 Gm.) tablets every four hours and to avoid sunlight. She did this for two weeks, during which time she felt weak. After she had taken about eighty tablets an extremely pruritic erythematous eruption appeared on her extremities; her face became swollen but not red. She discontinued the pills for several days. A week later she was advised to take one tablet four times a day. Ten minutes after taking the first dose the pruritus and the eruption became aggravated. The medication was discontinued, and the eruption faded. In ten days (by July 15) it disappeared entirely. About August 1 she went to the beach for a day and suffered a severe sunburn, which confined her to bed for three days. She states that the present eruption, which began about the end of September, corresponds to the areas most severely affected by the sunburn. She now presents a dusky erythematous eruption on the nose and cheeks and along the hair line. There are no lesions of the mouth.

DISCUSSION

DR. ISADORE ROSEN: This case is interesting, because in the last year or so a number of dermatologists have been reporting good results in cases of lupus erythematosus from the use of sulfanilamide and here the drug produces this disease.

DR. DAVID L. SATENSTEIN: I think Dr. Rosen is wrong. Dr. Sharlit has recently reported that sulfanilamide will make the skin sensitive to sunlight, and if that is true lupus erythematosus can develop from it, but I should not say that sulfanilamide is the cause of the lupus erythematosus. The skin is sensitive to sunlight, and then lupus erythematosus develops. The patient starts off with that sensitivity before the sulfanilamide is used. I should not blame the drug.

DR. E. WILLIAM ABRAMOWITZ: It is known that the gold compounds used in the treatment of lupus erythematosus are also photosensitizing agents. Among other drugs that possess such properties are the barbiturates. Whether the eruption that this patient presents is a result of taking sulfanilamide is a question. It would be interesting to give this patient sulfanilamide later to see if the eruption reappears. I presented a patient (ARCH. DERMAT. & SYPH. **39**:367 [Feb.] 1939) who some of the members thought might have an unusual form of lupus erythematosus. On a number of occasions, as long as sulfanilamide was given the eruption almost disappeared, but as soon as the drug was stopped the eruption promptly returned. The eruption even disappeared after a hemorrhoidectomy, but after a while it returned. The patient was given sulfanilamide again, with the usual improvement of the cutaneous eruption.

DR. PAUL E. BECHET: The patient has many definite symptoms of the early discoid type of lupus erythematosus. The lower margin of the lesion on the nose is sharply defined and scaly, with patulous follicular openings, and there is infiltration. The lesions, therefore, do not of themselves suggest the disseminate type. Excessive actinic light alone is a decided factor in the causation of lupus erythematosus. In my experience this has been proved time and time again.

There is an increase in the incidence of the disease during or immediately after the summer. Patients have repeatedly come under my observation with acute lupus erythematosus following blistering exposures to sunlight. In at least half a dozen cases the eruption occurred after a severe burn from radiation produced by an ultraviolet lamp. The recent increase of lupus erythematosus in children a few years old and the fact that these children visit the beach in so-called sun suits, practically nude, are more than a coincidence. I have observed in these same children patches of lupus erythematosus on the back, with adjacent exfoliation of the skin from severe sunburn.

DR. MAX SCHEER: I think sulfanilamide played an accessory role in this case, and the combination of the two factors rendered much more likely the development of lupus erythematosus.

DR. MAURICE COSTELLO: The interesting fact in the history of this patient is that with the exception of the sunburn the patient received less sunlight last summer than any other year, because she was told to avoid it. Since sulfanilamide is a photosensitizing drug, I believe that there is a causal relation between its use by this patient, followed by sunburn, and the appearance of the present eruption. If the acutely erythematous eruption now present on her face were accompanied by a similar eruption on the chest and extremities, I should not hesitate to make the diagnosis of acute lupus erythematosus of the disseminate type.

Lupus Vulgaris, Papulonecrotic Tuberculid, Argyria and Trichiasis. Presented by DR. ANTHONY C. CIPOLLARO.

M. B., a woman aged 47, born in Italy, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, service of Dr. Isadore Rosen on March 13, 1936, with a lesion on the right ala nasi of five weeks' duration. This lesion was the size of a dime, violaceous and somewhat infiltrated and had a moderate number of telangiectatic vessels on the surface. The histologic diagnosis was lupus vulgaris.

There were also about ten lesions on the lower extremities, each about the size of a pea. These were crusted nodules which resulted in scar formation. The diagnosis was papulonecrotic tuberculid. Tuberculin tests showed a 1 plus reaction with a 1 : 1,000,000, a 4 plus reaction with a 1 : 100,000 and a 4 plus reaction with bullous lesions with a 1 : 10,000 dilution.

For several years the patient had trachoma, which was treated with mild protein silver. After many years of treatment the conjunctivas became bluish gray. She now presents evidences of argyria involving only the conjunctivas.

Her most recent readmission to the hospital was for the treatment of trichiasis which followed trachoma. The patient was referred to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital by the ophthalmologic department for electrolysis.

DISCUSSION

DR. MAURICE COSTELLO: Last year I presented a young woman who had localized argyria confined to the conjunctivas. It has been stated that argyria always follows the internal administration of silver salts. Argyria following the instillation of mild protein silver in the nose is said to be caused by the absorption by the stomach of the silver salts thus swallowed. There must be some local absorption by the tissues at the site of first contact, as is proved by this case of localized argyria.

DR. LUDWIG OULMANN: I remember a case of argyria of the face in an elderly man who dyed his beard with a silver nitrate solution. I presented the patient here years ago.

DR. E. WILLIAM ABRAMOWITZ: This patient had trachoma and may have an occlusion of the tear duct. In that case the chances of the drug's getting into

the nose and into the mouth were small, so that the argyria would be limited to the particular area where the drug was applied.

DR. MIHRAN B. PAROUNAGIAN: I think the most pronounced argyria I have even seen was in a case presented before this society from my service at Gouverneur Hospital many years ago. The patient was a mature woman who had some pharyngeal disease for which a physician had prescribed silver nitrate solution. She had been applying this for a long time. When seen by me she resembled a bronze statue. This subject interests me because when I began the use of silver arsphenamine at Bellevue Hospital in October 1920, many physicians expressed fear of argyria; in fact, some textbooks mentioned that possibility. However, I must say that out of thousands of injections administered in my department at Bellevue Hospital, as well as in my private practice, I have never encountered a single case of argyria. I must state here that the dose was never more than 0.2 Gm.

DR. E. WILLIAM ABRAMOWITZ: Argyria following the use of silver arsphenamine is reported usually after three or four courses are given, with the larger dose of 0.3 Gm. Several years may pass before symptoms of argyria develop.

DR. J. FRANK FRASER: In Gaul's investigation it was found that any amount over 8 Gm. of silver arsphenamine would produce argyria.

Granuloma Annulare. Presented by DR. ANTHONY C. CIPOLLARO.

E. K., a woman aged 21, born in the United States, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, service of Dr. Isadore Rosen, on July 13, 1938. She complained of a lesion situated on the back between the scapulas, of two years' duration. The lesion is round and slightly elevated and has a clear center. It is sharply demarcated. The color is slightly pinker than that of normal skin. The patient has received two roentgen treatments, one on July 13 and one on September 14. Each treatment consisted of 300 roentgens without filtration. After these treatments there was no improvement.

DISCUSSION

DR. FRED WISE: The lesion resembles granuloma annulare, but it does not have the typical features of that condition. I think it is lichen albus of von Zumbusch. I shall be interested to hear what the microscopic examination shows.

DR. MAURICE COSTELLO: I should expect granuloma annulare to respond rather promptly to the dose of roentgen rays administered to this lesion. I agree with Dr. Wise that this patient has lichen albus of von Zumbusch.

DR. MIHRAN B. PAROUNAGIAN: I should make a tentative diagnosis of scleroderma in the early stage. The histologic examination showed granuloma annulare. The lesions disappeared after the third roentgen treatment.

Lichen Planus Involving Only the Labia Majora and the Buccal Mucous Membrane. Presented by DR. MAURICE COSTELLO.

M. S., a married woman aged 46, a housewife, Hungarian by birth, has nine children living and well. An eruption on the labia, with accompanying pruritus, has been present about nine weeks. The duration of the lesions on the buccal mucous membranes is unknown, the patient having been unaware of their presence. The lesions on the labia consist of many pinhead-sized to pea-sized grayish excoriated lesions with slight infiltration. The lesions of the buccal mucous membrane consist of grayish white streaks, dots and circles, a reticulated network of strands and bands.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: One of my patients had lichen planus of the larynx associated with her cutaneous lesions.

BRONX DERMATOLOGICAL SOCIETY

SAMUEL M. PECK, M.D., *President*

Oct. 27, 1938

HENRY SILVER, M.D., *Secretary*

Pemphigus Treated with Sulfanilamide; Sulfanilamide Eruption. Presented by DR. SAMUEL FELDMAN.

Mrs. E. S., a housewife aged 57, began to complain of weakness and dizzy spells in the summer of 1937. She became irritable, felt a burning sensation in the chest and complained of pain in the throat, particularly on swallowing. In January 1938 red spots appeared on the back of the tongue, and a bulla was detected on the roof of the mouth. The condition was diagnosed elsewhere as Vincent's angina. The patient had lost about 30 pounds (13.6 Kg.) during the preceding five months, and the condition of the mouth became gradually worse.

Early in March 1938 the diagnosis of pemphigus was established. Arsenicals and injections of liver extracts failed to check the progress of the disease. After these injections bullae developed on the buttocks at their sites. From that time on new blebs appeared, and on May 24 the patient was admitted to the Bronx Hospital. Her body was covered with bullae, which ruptured, leaving numerous denuded areas or areas covered with macerated epithelium having an offensive odor. There were several deep ulcerations on the buttocks. The patient was emaciated, weak and at times semiconscious. The pulse rate was 98, the respiratory rate 22 and the temperature 98.8 F. The blood and urine showed no abnormalities.

At the hospital the patient was given five intravenous injections of germanin, one every five days, without improvement. If anything, the condition became worse. About the middle of June the germanin was discontinued, and sulfanilamide by mouth was substituted. The patient was given three 5 grain (0.32 Gm.) tablets three times a day for three days, then two tablets three times a day and finally one tablet three times a day. The urine and blood were examined every three days. Almost immediately after the beginning of the sulfanilamide treatment the patient began to improve, and she was free of lesions in about three weeks. At that time the medication consisted of only 5 grains (0.32 Gm.) of sulfanilamide daily. On July 8 she had a chill, became drowsy and had a temperature of 103 F. Sulfanilamide was discontinued. Two days later the face became red and swollen. The glands in the neck were palpable and tender; the ankles were swollen, and gradually an intense erythema developed. The eruption was not unlike that of scarlet fever except that the color was much darker. Later, a minute papulovesicular eruption appeared. The peculiar feature of the eruption was that it did not occur in any of the areas which had been previously attacked by pemphigus. There was pharyngitis, and the patient complained of pain on swallowing and a burning sensation of the skin when she came in contact with the bed or bedclothes. She had difficulty in urination and had to be catheterized every day for a week. The temperature and the eruption gradually subsided, and the skin healed, with desquamation. Complete casts of the palms and soles were thrown off. The patient was discharged from the hospital on August 2. At that time she felt much stronger, and her appetite was good. Walking was impeded because of arthritis, which developed either simultaneously with or as a result of the sulfanilamide reaction.

Early in September a new bleb appeared on the tongue. In the hope that the patient might tolerate small doses of sulfanilamide, the drug was again prescribed. Four hours after she had taken one 5 grain (0.32 Gm.) tablet an eruption appeared, accompanied by swelling of the face, fever and other manifestations of severe reaction, which cleared up in about one week. At that time there were a small bleb on the tongue and a seropurulent discharge from the navel.

On October 13 she was given ½ grain (0.03 Gm.) of sulfanilamide to test her tolerance of the drug. The previous improvement was so clearly due to the drug that it was felt that some good might be derived if she could tolerate even minute amounts. However, one hour after administration of the drug she had fever; her face became swollen, and an eruption appeared over her entire body. There was the same difficulty in urination and deglutition as during the first attack. The similarity of the three attacks suggests the possibility that this type of reaction is characteristic for sulfanilamide.

DISCUSSION

DR. CHARLES WOLF: Recently I have treated with sulfanilamide a patient suffering from pemphigus. The disease responded favorably in the beginning but soon became resistant to this therapy. Sulfanilamide may be of benefit during the acute stage. I feel that it will not permanently influence the disease.

DR. PAUL GROSS: The results obtained by Dr. Feldman in this case are excellent. I have used sulfanilamide for an extensive bullous eruption, with most unfavorable results. The patient required numerous blood transfusions, and the condition finally cleared up after liver therapy. So far, treatment of pemphigus with any new drug has been unreliable, giving good results in the first few cases and no results in subsequent cases. In other words, nothing as yet has been found that even approaches specific therapy. Therefore, reliance on the complete armamentarium of pemphigus therapy is essential.

DR. LOUIS CHARGIN: I think that Dr. Feldman should be congratulated on the excellent results obtained with the use of sulfanilamide in this case. This is the third case of pemphigus that I know of in which sulfanilamide was beneficial. All physicians realize that pemphigus is a serious disease. Any new remedy that offers a hope of cure should be given the best possible trial. Sulfanilamide now and then causes toxic symptoms, as I have had occasion to observe; fortunately, such symptoms are rare. The arsphenamines, for instance, produce a toxic reaction, but for that reason alone one would not discontinue their use. I do not suggest that sulfanilamide should be given in large doses in all cases, but it should be given in the largest possible dose consistent with safety.

DR. DAVID BLOOM: In the few cases I have observed of pemphigus treated with sulfanilamide the condition did not respond to the drug.

DR. ADOLPH ROSTENBERG: There is no question that sulfanilamide is a valuable drug in many diseases, but I see its downfall already because of its indiscriminate use. My feeling is that the course this drug will take in the treatment of pemphigus will parallel that of methylthionine chloride (methylene blue). There was enthusiasm at first because of the good results obtained in 2 cases. The treatment proved disappointing, however, on further trial.

I have recently observed a patient suffering from carcinoma of the gastrointestinal tract and pemphigus. The association of carcinoma and pemphigus is interesting.

DR. MOSES H. HOLLAND (by invitation): A patient with pemphigus who is under my care at present was treated with large doses of sulfanilamide, but the disease became aggravated. The drug was tried on several occasions during a period of about four months. It should, however, be pointed out that the patient also failed to respond to germanin.

DR. MARION B. SULZBERGER: I have tried sulfanilamide in a few cases of pemphigus, without beneficial effect. I used the drug in both small and large doses. This does not mean that there will not be an occasional patient who will respond favorably. Moreover, related compounds, such as dimethyldisulfanilamide (4-[4′-aminobenzenesulfonamido]-benzenesulfonedimethylamide), which has proved effective for gonorrhea, and the pyrazolon derivative (sulfapyridine) which has proved valuable in pneumococcic infections (pneumonia), should all be tried for pemphigus and other ordinarily fatal cutaneous diseases. Nevertheless, so far the statistics on germanin show that it is one of the best remedies for pemphigus,

although it is of course not nearly good enough. When one begins to use new drugs, such as sulfanilamide, one has a wonderful opportunity to observe that many of the untoward reactions to drugs are on an allergic basis. For instance, this particular patient tolerated relatively large amounts of the drug for a considerable time and then became suddenly so sensitive to it that she could not take even small amounts. This is obviously an instance of specific acquired sensitivity or allergy and not one of cumulative toxic effect.

DR. CHARLES LERNER: Since this patient shows such marked sensitivity to sulfanilamide it is conceivable that the improvement may be not so much the effect of the drug itself as the effect of the shock mechanism; in other words, that the reaction may have greater curative power than the drug per se.

DR. SAMUEL FELDMAN: The improvement in this case was dramatic and followed closely the administration of sulfanilamide. I never saw that before. In the cases in which methylthionine chloride was used the eruption required months to clear up. However, the patient had several severe reactions. Full doses of sulfanilamide may be given without fear of such complications as agranulocytosis if the patient is watched and the blood is examined repeatedly. It is necessary to emphasize that this patient improved long before the reaction occurred, and that is why the improvement cannot be ascribed to the reaction.

Epidermolysis Bullosa in Mother and Child. Presented by DR. LOUIS CHARGIN.

P. C., a girl aged 10 weeks, the first child of her parents, presents an eruption which appeared soon after birth and has since persisted. The lesions are large, clear hemorrhagic bullae which rupture rather readily, leaving superficial erosions. The eruption is located on the feet, knees, hands and abdomen. All types of bullae in all stages can be seen. There is no dystrophy. The child's general health is good.

The mother is likewise affected, but to a much less extent and degree. She shows scattered lesions which may have been produced by trauma.

DISCUSSION

DR. ADOLPH ROSTENBERG: I was so fortunate as to see this baby two days after birth and learned that the eruption had been present at birth. The region over both ankles was denuded, and the obstetrician made a diagnosis of pemphigus neonatorum, to which the eruption bears a strong resemblance. The mother was suffering from the same disease, and this fact helped to establish the diagnosis. In most of the recorded cases symptoms have been present in early life but not at birth. Intrauterine traumatism must play a role in this condition. With regard to treatment, it was ascertained that pituitary extract has been used in some cases. I should like to inquire regarding the prognosis for so young an infant.

DR. MAX BERKOVSKY: I saw the infant two days after delivery. Clinically the eruption resembled mild bullous impetigo. In the few cases of epidermolysis bullosa that I have observed, I have never been able to find the disease in the father and mother. This is the first case I have observed in which mother and infant are affected.

DR. HENRY SILVER: I also saw the infant a few days after birth, and already at that time there were definite changes of the toe nails, such as longitudinal and transverse ridges, brownish discoloration and partial onycholysis. These changes, which are more pronounced today, were helpful in establishing the diagnosis.

With regard to therapy, I suggest large doses of viosterol. Some years ago J. B. Ludy, of Philadelphia, claimed good results with this type of therapy in bullous diseases like pemphigus and epidermolysis bullosa. In view of the need for large doses and the age of the infant, caution is necessary.

DR. WILBERT SACHS: One would accomplish something with therapy in epidermolysis bullosa if the elastic tissue could be replaced.

DR. LOUIS CHARGIN: When I saw the child she was about 6 weeks old. Although the diagnosis of epidermolysis bullosa seemed definite, syphilis had to be ruled out. In syphilis the child is undernourished, and almost always one sees an associated infiltration of the skin with the bullae, which is not present in this case. As a rule, bullae of syphilis are seen on the palms and soles, while in this case they are located on areas subject to trauma. In bullous impetigo the eruption is not limited to traumatized areas and is uncommon on the palms and soles.

In answer to Dr. Rostenberg's inquiry, the prognosis is not as bad as it appears. The mother is about 38 years old, has had the disease since early life and is otherwise in excellent health. The prognosis is bad only in cases in which there is dystrophy, and so far there are no signs of dystrophy in this child. There are no changes except that bullae develop on trauma. The child will probably go on having bullae but will otherwise develop normally.

Changes in the elastic tissue are not present in all cases. They are not present in so-called simple epidermolysis bullosa. I do not know whether destructive changes will develop in the elastic tissue in this case. With regard to therapy, I shall be glad to follow the suggestion of Dr. Silver.

Granulosis Rubra Nasi. Presented by DR. LEO SPIEGEL.

M. H., a clerk aged 21, single, presents an eruption on the cartilaginous portion of the nose, of about twelve years' duration. There is a well defined area of redness, the borders of which are fading gradually. On the erythematous area there are numerous densely set tiny papules with interspersed beads of perspiration. There are no subjective symptoms, but the condition is disfiguring, and the patient is made self conscious by his facial appearance. The case is presented for suggestions as to therapy.

DISCUSSION

DR. CHARLES WOLF: If therapy is required, it seems to me that roentgen treatment is advisable. By drying up the sweat glands one can remove the troublesome symptom, excessive sweating, and thereby improve the appearance.

DR. ADOLPH ROSTENBERG: Roentgen therapy as used for acne seems to be the logical method.

DR. MARION B. SULZBERGER: In my cases roentgen rays have helped temporarily when a series of eight to ten ¼ skin unit (75 roentgen) doses were given to the nose. Ordinarily, after this treatment the sweating is reduced and the nose looks definitely paler. The condition usually recurs in a few months.

DR. LEO SPIEGEL: I have used roentgen rays, and I also gave eight to ten ¼ skin unit (75 roentgen) doses, without obtaining any result. Various ointments and soothing applications have been used without benefit. A form of therapy that should not be used in this disease is electrodesiccation, for it leads only to scar formation and disfigurement, as is evident in this case.

Generalized Neurodermatitis with Cataract Formation. Presented by DR. SAMUEL M. PECK.

T. M., a truckman aged 23, born in the United States, was admitted to the clinic of the Mount Sinai Hospital on July 16, 1928, at the age of 12 years. He then presented an erythematous and papular eruption with lichenification of the skin, involving the cubital regions, the axillas and the upper part of the chest. The eruption was associated with itching. On Dec. 16, 1930, he presented typical neurodermatitis of the flexures of the arms and legs, the axillas, the face and the neck.

On Aug. 5, 1938, physical examination showed that the status was generally unchanged. There was a generalized eruption involving the body, extremities, face and scalp. The eyebrows were sparse and short. The entire body was

pigmented. There was a generalized maculopapular erythematous eruption with scaling and crusting. The skin was thickened, coarse and lichenified and showed numerous scratch marks. There were a few scattered pustules over the face and body.

The patient was given six hyperthermal treatments, during which his temperature was raised to 103 F. for two hours. The right eye showed opacity in the lens during the course of treatment. The cutaneous condition improved, the pruritus disappeared and the lesions receded. The patient was discharged to the physical therapy follow-up clinic and instructed to return for monthly hyperthermal treatments. On September 8 examination by an ophthalmologist revealed a fairly mature change in the right lens. Vision in the left eye was 20/20.

The intradermal test with trichophytin gave a negative reaction after forty-eight hours. Tests with mercury bichloride in a dilution of 1:1,000, trinitrophenol, formaldehyde, turpentine and quinine all gave negative reactions.

Examination of the blood showed 91 per cent hemoglobin. The leukocyte count was 13,700, with 7 per cent eosinophils. Urinalysis gave negative results.

DISCUSSION

DR. MARION B. SULZBERGER: I think physicians have come to recognize that the association of cataracts with severe atopic dermatitis is much more common than was at first supposed. I think the members will recall 2 cases of this association which I presented before the society (ARCH. DERMAT. & SYPH. **34**:328 [Aug.] 1936; **35**:368 [Feb.] 1937). I believe that this patient must have had some disposition toward cataracts, as they matured so rapidly under fever therapy. In 1 of my cases there was extremely rapid progression of the cataract without fever therapy. The interesting thing about this boy is that he, like so many patients with this condition, has improved every time he has been hospitalized. His improvement in the hospital was just as rapid when he received fever treatment as when he did not, and that is another common and mysterious observation in cases of atopic dermatitis. I should like to refer again to the medical student whom I presented before this society (ARCH. DERMAT. & SYPH. **34**:328 [Aug.] 1936). The progression of the cutaneous disease and of the cataracts was rapid in spite of all therapeutic efforts. As soon as the patient completed his medical course I advised him to leave New York and travel until he found a place where he felt well. After trying out many localities he settled at a beach resort 20 miles (37,065 M.) from San Diego, Calif. There the itching stopped almost immediately, and the eruption began to clear up without any other change in manner of living, diet or medication. After a stay of six months he returned to New York. Examination showed only slight pigmentation and thickening of the previously affected areas. He then had the cataract removed and has remained well for one year.

DR. ADOLPH ROSTENBERG: It is important to record that there is no relation between the cataracts observed in patients with atopic dermatitis and roentgen therapy, though such a relation has been assumed by some.

DR. LOUIS CHARGIN: Because of Dr. Peck's suggestion of the possible development of the cataract after fever therapy, I looked up the literature and found that the first case of cataract associated with eczema was reported in 1868. Since then a number of cases have been recorded. In other words, before hot box therapy or fever therapy was introduced and before roentgen therapy was employed the association was already known. Cataracts occur in association with a variety of cutaneous diseases, such as generalized telangiectasia, alopecia areata and scleroderma. One must also bear in mind that when patients receive fever therapy the head is outside the box and the eyes are not directly subjected to the heat.

DR. SAMUEL M. PECK: I wish to stress the point that this case is not presented as an instance of a complication of fever therapy producing cataracts in neurodermatitis. It is known that in India cataracts are frequent. The consensus as to their cause is that it is not so much the hot climate as the peculiar effect of

the actinic rays in that country. On the other hand, it is known that heat plays a role in the formation of cataract. This is seen in connection with glass blowing and other occupations in which the worker is exposed to high temperatures.

Extensive Granuloma Inguinale. Presented by Dr. G. D. Astrachan.

F. C., a Negro aged 48, was admitted to the Metropolitan Hospital on Aug. 26, 1938, presenting an eruption in the inguinal region, accompanied with pain. The condition began approximately eight years ago, when a diagnosis of granuloma inguinale was made and treatment, consisting of "hip injections," instituted. These resulted in nearly complete subsidence of the cutaneous manifestations. Since that time numerous exacerbations and regressions have occurred.

Over the entire pubic region and extending laterally over both inguinal regions and the upper half of the scrotum and involving the penis is a well defined area, presenting in parts an ulcerative growth and in parts areas of thick scar tissue. The border of the entire lesion is hard and infiltrated, and the ulcerative portions present evidence of a moderate amount of seropurulent discharge. The more central scarred atrophic areas are hard and bound to the underlying tissues. The penis is reduced to a stump about 1½ inches (3.7 cm.) in length. A similar but smaller area presenting hypertrophy and considerable granulation tissue is located on the lower portion of the buttocks and the upper third of the scrotum posteriorly. The scrotum is enlarged to about four times the normal size. There is no disturbance of bowel action or of urinary function.

Serologic and chemical examination of the blood gave essentially negative results, as did urinalysis. The Frei test gave a negative reaction. Examination of the blood showed 60 per cent hemoglobin, 3,360,000 red cells and 5,700 white cells. The differential count showed 57 per cent polymorphonuclear leukocytes, 40 per cent lymphocytes, 2 per cent monocytes and 1 per cent eosinophils.

DISCUSSION

Dr. David Bloom: Elephantiasis of the scrotum is a feature of granuloma inguinale in some cases. It may be so severe that the whole penis is covered by the scrotum and only the meatus urethrae is visible.

Dr. G. D. Astrachan: Of interest is the patient's response to therapy. Fuadin failed to improve the condition. Because of the definite anemia, liver therapy was given in addition to the injections of fuadin, with an excellent response in three weeks.

A Case for Diagnosis (Dermatitis Medicamentosa?). Presented by Dr. Henry Silver.

R. S., a Negress aged 44, the mother of three children, came to the clinic of the Mount Sinai Hospital on Jan. 11, 1934, presenting a scattered erythematous eruption of one year's duration. The lesions were mostly macular; some were papular or urticarial, first involving the lips and chin and then spreading to the chest, arms, hands, back and hips. On the chest and arms were, in addition, areas of hyperpigmentation and sharply defined areas of depigmentation. These peculiar changes in pigment followed healing of erythematous areas. Questioned about the ingestion of drugs, the patient said she had taken "alophen" pills (containing aloin, strychnine, extract of belladonna, ipecac and phenolphthalein). A test, however, with phenolphthalein gave negative results. A test with phenobarbital also gave negative results. The Wassermann reaction was negative.

The blood count showed 4,500,000 red cells and 10,900 white blood cells, with 62 per cent polymorphonuclear leukocytes, 35 per cent lymphocytes and 3 per cent mononuclears. Urinalysis showed many urates but gave otherwise negative results. Examination of the feces failed to reveal intestinal parasites.

Histologic examination of a lesion from the right forearm showed hyperkeratosis but no parakeratosis. The lower layers of the epidermis showed edema, both intracellular and intercellular, with invasion by leukocytes at various points; the

underlying cutis showed the same acute process, with edema, vascular dilatation and pronounced infiltration with leukocytes and lymphocytes. There was marked edema of the fibrillar structures. Pigment was seen in clumps free in tissue as well as in wandering cells. This picture suggested toxic erythema or erythema multiforme.

A course of twelve injections of autoblood was given, after which the eruption markedly improved.

By the end of 1934 new lesions appeared, which healed with superficial atrophy. The lesions were suggestive of lupus erythematosus. Biopsy of material from a lesion which included an area of depigmentation showed hyperkeratosis with only a moderate degree of thinning of the epidermis. There was no real atrophy immediately below the epidermis. There was a marked inflammatory reaction, consisting mainly of lymphocytes and polymorphonuclear leukocytes, and there was telangiectasis. There were no changes in the elastica other than a marked inflammatory reaction. There were no basophilic changes in the cutis. The epidermis showed areas of depigmentation. There were no chromatophores in the cutis. The diagnosis was multiforme erythema.

From Nov. 1, 1934, unil April 1935 the patient received sixteen injections of sodium gold thiosulfate (10 mg. per dose).

On April 4 a new crop of lesions appeared on the thighs and legs. The lesions were erythematovesicular, slightly raised and the size of a twenty-five cent piece or larger; they itched considerably. The possibility of a dermatitis due to gold medication was considered, and the drug was discontinued. Since then the patient has had remissions and periodic exacerbations.

At the end of September 1938 there was a great deal of activity in the older lesions. There were many areas of depigmentation. The sacral region showed atrophy. This time the patient stated that six weeks ago her body was completely free of eruption. To relieve constipation she took three "ex-lax" tablets. In the following forty-eight hours the eruption appeared all over her body. She previously had taken "feenamint" and "alophen" tablets.

A test with 1 grain (0.06 Gm.) of phenolphthalein for two days caused a definite flare-up of the lesions, which became redder and more itchy. Fresh lesions, red and edematous, appeared on the upper lip.

DISCUSSION

DR. ARTHUR SAYER: Dr. Silver stated that phenolphthalein caused a definite flare-up of the lesions. Is not that phenomenon proof that phenolphthalein is the underlying factor in this case?

DR. MARION B. SULZBERGER: I incline strongly to the diagnosis of disseminated discoid lupus erythematosus. The question is whether the flare-up of the lesions after the administration of phenolphthalein proves that they were originally due to that drug. It is known that there are "nonspecific" flare-ups after administration of drugs or of biologic allergens. Conversely, I am not convinced that negative results of such clinical tests mean that the eruption was not caused by the drug. There may be refractory stages, temporary local desensitizations or anergic states. The opposite, i. e., the nonspecific flare-ups, are less frequent. I do not know of an instance in which such a nonspecific flare-up has occurred with phenolphthalein, but it often occurs with iodides or arsphenamine. Moreover, even in lupus erythematosus one finds local reactions in the lesions after the administration of a drug such as a gold compound. Many dermatoses in which one cannot consider a drug as a definite etiologic factor will have focal reactions and flares when iodides or bromides are administered. I refer you, for example, to the Jarisch-Herxheimer reaction in syphilid, to flare-ups of dermatitis herpetiformis and of acne vulgaris after ingestion of iodides, bromides or chocolate and of herpes simplex after ingestion of drugs or foods and to other examples of such synergistic effects. All of these observations impel me to the conclusion that one cannot say, just because lesions flare up after administration of a drug, that they were actually caused by that drug.

DR. SAMUEL M. PECK: Has any one ever seen phenolphthalein produce a flare-up of a fixed arsphenamine eruption?

DR. LOUIS CHARGIN: It seems to me that the diagnosis in this case may possibly be established with the aid of histologic study. On purely clinical grounds it seems impossible to establish a diagnosis. This eruption reminds me of the type which is occasionally observed after arsphenamine dermatitis, which, when it clears, leaves somewhat atrophic areas surrounded by pigmented borders.

DR. HENRY SILVER: I think that Dr. Sayer's question has been adequately answered by Dr. Sulzberger. One has to admit that the diagnosis is not clearcut. I agree with Dr. Sulzberger that the flare-up following the administration of phenolphthalein does not prove that the eruption is due to the drug. On former occasions it was impossible to activate the lesions of this patient with phenolphthalein. Another possibility which one must take into consideration is that this condition is superficial lupus erythematosus activated by phenolphthalein. I do not think that another biopsy will be helpful.

Leukodermic Macular Atrophy Probably Due to Secondary Syphilis. Presented by DR. MARION B. SULZBERGER.

E. B., a housewife aged 56, states that she had a scaly eruption on the back and shoulders about thirty years ago, which disappeared in ten days with use of an ointment.

About this time the patient was treated by her family physician with a course of weekly intravenous medication, followed by intragluteal injections. The patient was well until January 1938, when a diagnosis of syphilis of the central nervous system (type of dementia paralytica) was made at White Plains Hospital, White Plains, N. Y. She was transferred to Grasslands Hospital, Valhalla, N. Y., for more adequate treatment. The Wassermann reaction of the blood was repeatedly negative. The spinal fluid showed a faint trace of globulin, a 4 plus Wassermann reaction and a colloidal gold curve of 1123321100.

On July 28 she was admitted to Montefiore Hospital for Chronic Diseases, where the diagnosis of syphilis of the central nervous system was confirmed. A diagnosis of leukodermic macular atrophy, probably following a secondary syphiloderm, was also made.

There are numerous discrete oval to circular depressed lesions, varying from 0.5 to 1 cm. in diameter, on the back, shoulders and arms. The lesions are ivory to grayish white and are smooth surfaced. When puckered they show marked wrinkling.

DISCUSSION

DR. HENRY SILVER: I am inclined to accept a diagnosis of macular atrophy. For confirmation of the clinical impression histologic study should be made. It is, however, easy to identify clinically some of the lesions as macular atrophic spots. Of interest in this case is the leukodermic aspect of the lesions. White, depigmented macular atrophic spots follow usually in the wake of syphilitic eruptions. Fournier was the first to call attention to them and suggested the name *leucatrophie cutanée*. The patient had syphilis many years ago and states that the "spots" developed at the site of the syphilitic eruption. Therefore, it is logical to assume that the condition is syphilitic macular atrophy with depigmentation.

DR. MARION B. SULZBERGER: While I do not believe the condition is by any means typical macular atrophy and do not believe that all the lesions can be diagnosed as macular atrophy, I agree with Dr. Silver that there are enough characteristic lesions of macular atrophy with depigmentation to justify the diagnosis.

A Case for Diagnosis (Schamberg's Progressive Pigmentation?). Presented by DR. SAMUEL FELDMAN.

K. S., a housewife aged 69, states that about six years ago she noticed that small red spots appeared on the ankles, followed soon by lesions on the legs and

thighs. The lesions appeared in crops; some became ulcerated and healed, with round, smooth scars. During the course of years new lesions would appear and heal in the same manner or leave marked pigmentation, particularly on the anterior aspect of each leg and about the ankles.

On the legs and the anterior surfaces of the thighs there are numerous cayenne pepper-like spots. No dilated vessels are seen. Scattered here and there are several purpuric areas. The larger ones show a tendency to break down and ulcerate. Pigmentation in patches is present on both legs, particularly on the shins. The skin in that region shows a tendency to atrophy.

Histologic examination of a lesion taken from the thigh, which included cayenne pepper spots, showed hyperkeratosis but no parakeratosis. The granular layer was normal. The rete consisted of only two to four layers. No rete pegs or papillae were present in the section. The upper layer of the cutis consisted of loose connective tissue bundles. The blood vessels were dilated. In a number of them the endothelium was thickened. There was an almost solid perivascular infiltration, consisting of round cells and a few fibroblasts. No red blood cells or blood pigment were found.

DISCUSSION

DR. LOUIS CHARGIN: I do not wish to make a definite diagnosis in this case without further study. I can say, however, that the eruption does not strike me as either Majocchi's disease (purpura annularis telangiectoides) or Schamberg's disease. In the few cases of real Majocchi's disease that I have observed the lesions were purpuric, more or less round, not numerous and usually located below the knee. There was no associated varicose vein complex. In Schamberg's disease the process resembles the end stage of dermatitis haemostatica. As a provisional diagnosis I should consider a dermatitis on the basis of a varicose vein complex.

DR. LEO SPIEGEL: I do not believe the condition is either of those mentioned. It brings to my mind the usual controversy attending such pigmentary dermatoses. It is difficult to say what it is. It impressed me as a varicose complex. There has been altered circulation, with a small superficial gangrenous ulcer and with resulting pigmentary changes in the lower part of the leg.

DR. CHARLES LERNER: It is plausible to suppose that Majocchi's disease can occur superimposed on previous or concomitant dermatitis haemostatica, especially in a woman as old as this patient. I was able to discern, besides the dermatitis haemostatica, definite purpuric annular and telangiectatic lesions.

DR. WILBERT SACHS: There were no pathologic features of Majocchi's disease on histologic examination. The atrophy present is to be expected in a patient 70 years of age.

DR. SAMUEL M. PECK: Many physicians have been confused many times in trying to differentiate between Majocchi's disease, Schamberg's disease and angioma serpiginosum. The more one reads the existing literature, the more confusing the whole subject becomes. The main point of difference seems to be based on histologic grounds; namely, whether there is an obliterating disease of the vessels or only an inflammatory reaction. According to Majocchi's original paper, young males are mostly affected. This is also true of Schamberg's disease, while with angioma serpiginosum females are mostly affected. While Wise and others have tried to establish many differential points, the diagnosis is still not as easy as is maintained. I think it is correct to state that this condition is a capillary disease, usually of the lower extremities. It is still to be decided whether the whole group do not represent variants of dermatitis haemostatica. The greatest criticism which can be raised against the differential histology is that it is impossible to define the pathology of capillary disease from one biopsy specimen from one region.

DR. SAMUEL FELDMAN: I, too, was not in favor of either diagnosis, but I am sure that the condition is not dermatitis haemostatica. In the first place, there are no evident varicose veins. Secondly, the telangiectatic lesions have been

stationary on the upper parts of the thighs for the last four months. There is no dermatitis in that region.

Lupus Erythematosus Treated with Sulfanilamide. Presented by DR. MARION B. SULZBERGER.

CASE 1.—W. C. K., a middle-aged man, presents an eruption on the back, arms and cheeks of about six years' duration. It was diagnosed at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in March 1937 as lupus erythematosus of the chronic disseminated discoid type.

The patient had received elsewhere injections of a bismuth preparation, manganese and sodium gold thiosulfate. These had no effect on the condition. Sulfanilamide medication was instituted in January 1938, in doses of 5 grains (0.32 Gm.) at first three times and later twice a day, and was discontinued in May 1938 because of the development of an erythematous eruption on the thighs and buttocks, which disappeared when the drug was discontinued. The patient improved remarkably on this treatment. Since then he has been receiving injections of sodium gold thiosulfate (5 to 10 mg.), with no benefit. Recently he has had treatments by gold ionization and is now beginning to show improvement.

The diagnosis after histologic examination on March 25, 1937, of a lesion removed from the left arm was of a late stage of lupus erythematosus. Examination of a lesion from the left side of the neck showed atypical lupus erythematosus.

Roentgenograms of the chest showed moderate old hilar thickening and scars of an old isolated puerile type of tuberculosis. The Wassermann and Kahn reactions were negative.

CASE 2.—S. H., a man aged 27, was presented before this society at the April 1937 meeting (ARCH. DERMAT. & SYPH. **37**:138 [Jan.] 1938).

In May sulfanilamide (5 grains [0.32 Gm.] three times a day) was administered. The condition improved, and after four months of treatment the lesions became inactive. In August sulfanilamide was discontinued, and a course of thirteen injections of a bismuth compound was given. The condition remained unchanged. Sulfanilamide was again administered in October, and again improvement occurred. In January 1938 the drug was stopped, and intramuscular injections of a bismuth preparation have been given since then.

DISCUSSION

DR. PAUL GROSS: I agree with those who favor a trial of small doses of sulfanilamide at the outset in conditions which do not require rapid action.

DR. DAVID BLOOM: Eight patients with lupus erythematosus (mostly of the chronic discoid type) who were given 15 grains (0.97 Gm.) of this drug daily did not respond to this treatment.

DR. LOUIS CHARGIN: I do not advocate the use of maximum doses as a routine. It is, however, safe to give maximum doses if required. If one can get a satisfactory response to 5 grains (0.32 Gm.) there is of course no reason to use 100 grains (6.48 Gm.). There has been a tendency to reduce the dose of sulfanilamide originally recommended. On the other hand, the majority of physicians still use large doses for gonorrhea, streptococcic infections or chancroid, in which diseases best results are obtained.

DR. ADOLPH ROSTENBERG: In the cases presented tonight was sulfanilamide administered alone, or was it given in conjunction with sodium gold thiosulfate?

DR. ISIDORE M. LASHINSKY: Considering that lupus erythematosus is a light-sensitive disease and sulfanilamide is a photosensitizer, I think that in order to prevent an exacerbation of the disease the patient must be instructed to avoid exposure to sunlight while under treatment.

DR. MARION B. SULZBERGER: I do not know how efficacious this drug is for lupus erythematosus in general, but it certainly was beneficial in these 2 cases and in a third case under my observation. Perhaps the eruptions in all 3 of these

cases could be called the subacute disseminate type rather than the discord type. In both cases other drugs were used, but not at the same time as sulfanilamide. With regard to Dr. Lashinsky's remarks, specific instructions to avoid sunlight are not given to all patients receiving sulfanilamide, but these 2 patients, because of the lupus erythematosus, did receive instructions to avoid it, even prior to receiving sulfanilamide. The new sulfanilamide derivatives merit a careful trial in lupus erythematosus, particularly those derivatives which have proved to be of special value in pneumococcic and gonococcic infections.

Purpura Annularis Telangiectoides (Majocchi). Presented by DR. ARTHUR SAYER.

H. G., a housewife aged 38, presented herself at the dispensary of the Morrisania City Hospital on June 14, 1938, with a diffuse eruption which was present mainly on the thighs and buttocks and to a lesser extent on the chest, arms and legs. She states that the eruption first appeared about six months ago and that it was gradually spreading in the location mentioned. She does not complain of itching or other subjective symptoms.

The lesions are macular, brownish and violaceous and the size of a pea and larger and show no scaliness. There is no definite grouping. Some of the lesions are definitely purpuric, and there is a suggestion of an annular arrangement. The Wassermann reaction was negative. Examination of the blood showed 80 per cent hemoglobin, 4,100,000 red cells and 13,000 white cells. The differential count showed 60 per cent polymorphonuclears, 40 per cent lymphocytes and 600,000 platelets.

During periodic observations it was noticed that the lesions became lighter in color and tended to disappear on the legs. At present most of the lesions are on the thigh and to a lesser extent on the arms, buttocks and lower part of the trunk. Permission for biopsy was refused.

DISCUSSION

DR. CHARLES WOLF: At first glance one might think of erythema ab igne. Another diagnosis to be considered is poikiloderma in the early stages, without the classic symptom of pseudoradiodermatitis.

DR. PAUL GROSS: If a biopsy specimen is taken I should suggest staining for amyloid. There is a rare type of amyloidosis in which the clinical features are similar to the lesions in this case (Marchionini, John: *Arch. f. Dermat. u. Syph.* **173**:545, 1936).

DR. SAMUEL M. PECK: I certainly should not think of Majocchi's disease in this case but should suggest Gougerot's lichenoid pigmented dermatitis.

I should like to mention again that I have obtained excellent results in this particular type of capillary disease with injections of snake venom.

DR. ARTHUR SAYER: I am aware that a case of this type should not be presented without a biopsy because the diagnosis depends so much on the characteristic histologic picture. Unfortunately, the patient refused permission for biopsy. I also had in mind poikiloderma. The eruption was never lichenoid; therefore, I do not think it is Gougerot's lichenoid dermatitis. It was always macular. There were definite cayenne pepper spots and an annular arrangement of some of the lesions. That is why I lean to the diagnosis of Majocchi's disease.

Pityriasis Lichenoides Chronica (Juliusberg). Presented by DR. ARTHUR SAYER.

L. S., a girl aged 18, born in the United States of Italian parentage, presented herself on October 10 at the dispensary of the Mount Sinai Hospital with a generalized eruption which was mainly localized on the trunk and upper extremities. She states that this eruption has been present for the past year and a half. It consists of small papules which vary in size from that of a pinhead to that of a split pea and are slightly red and somewhat scaly. There is no definite

grouping. Numerous small depigmented macular areas are scattered among the papular lesions mentioned. There are no subjective symptoms.

The Wassermann reaction of the blood was negative, and examination of the urine gave negative results.

DISCUSSION

DR. LOUIS CHARGIN: I think the condition is lichen planus.

DR. PAUL GROSS: It is worth while recording that the patient has pronounced leukoderma, especially in the posterior axillary folds. Both the acute and the chronic variety of pityriasis lichenoides are among the few diseases which may be accompanied with leukoderma verum. This is at times of diagnostic value.

DR. ADOLPH ROSTENBERG: I suggest the diagnosis of lichen planus.

DR. MARION B. SULZBERGER: There is no doubt in my mind that the lesions in this case are those of parapsoriasis en gouttes.

A Case for Diagnosis (Lupus Miliaris Disseminatus?). Presented by DR. FRANK E. CROSS.

R. F., a housewife aged 47, presents an eruption on both cheeks of six months' duration. A group of purplish maculopapular lesions the size of a pinhead or a small pea is located in the center of each cheek. Atrophic scarring is present.

Tuberculin tests with dilutions of 1:1,000,000, 1:100,000 and 1:10,000 gave negative results. The blood pressure was 200 systolic and 120 diastolic.

DISCUSSION

DR. MARION B. SULZBERGER: I think the condition is lupus miliaris disseminatus faciei of somewhat atypical appearance, with unusually small lesions. There are no rosacea-like lesions.

I should like to make a point with regard to tuberculin tests. If one performs quantitative tests, one should use a concentration of old tuberculin (Koch) as high as 1:10 if the preceding tests give negative results. One cannot speak of anergy unless the tests with a dilution of 1:1,000 and higher concentrations give negative results.

DR. FRANK E. CROSS: I am also inclined to the diagnosis of lupus miliaris disseminatus.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102–2d Ave., S. W., Rochester, Minn.
Place: New York. Time: Summer 1940.

Pan American Medical Association, Section of Dermatology and Syphilology

Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 49 Bay State Rd., Boston.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

Harold Orr, President, 10189–101st St., Edmonton.
Don Mitchell, Secretary-Treasurer, 1414 Drummond St., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1, England.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1, England.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

J. Bedford Shelmire, Chairman, 1719 Pacific Ave., Dallas, Texas.
C. F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.
Place: St. Louis. Time: May 15-19, 1939.

American Academy of Dermatology and Syphilology

Paul A. O'Leary, President, Mayo Clinic, Rochester, Minn.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: Philadelphia.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary-Treasurer, 416 Marlborough St., Boston.

American Dermatological Association

Francis E. Senear, President, 55 E. Washington St., Chicago.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.
Place: Seigniory Club, Montebello, Ontario, Canada. Time: May 1939.

Society for Investigative Dermatology

Joseph V. Klauder, President, 1934 Spruce St., Philadelphia.
S. W. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

George H. Belote, President, University Hospital, Ann Arbor, Mich.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.
Place: Pittsburgh. Time: March 25, 1939.

Mississippi Valley Dermatological Society

Hamilton Montgomery, President, Mayo Clinic, Rochester, Minn.
Herbert Rattner, Secretary-Treasurer, 25 E. Washington St., Chicago.
Place: Chicago.

New England Dermatological Society

Fred S. Burns, President, 83 Marlborough St., Boston.
B. Appel, Secretary, 483 Beacon St., Boston.

Northern New Jersey Dermatological Society

Francis McCauley, President, 31 Lincoln Pk., Newark.
Henri Abel, Secretary, 339 Union Ave., Elizabeth.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. L. Kirby-Smith, Chairman, 204 Laura St., Jacksonville, Fla.
Joseph A. Elliott, Secretary, Professional Bldg., Charlotte, N. C.

Southern Medical Association, Section on Dermatology and Syphilology

J. Richard Allison, Chairman, 1512 Marion St., Columbia, S. C.
Clinton W. Lane, Secretary, 508 N. Grand Ave., St. Louis.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Norman N. Epstein, Chairman, 450 Sutter St., San Francisco.
Arne E. Ingels, Secretary, 490 Post St., San Francisco.

Connecticut State Medical Society, Section on Dermatology

James D. Gold, Chairman, 839 Myrtle Ave., Bridgeport.
Albert Levenson, Secretary, 881 Lafayette St., Bridgeport.

Florida Society of Dermatology and Syphilology

Elmo D. French, Chairman, Huntington Bldg., Miami.
Lauren M. Sompayrac, Secretary, 459 St. James Bldg., Jacksonville.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

E. Lawrence Oliver, President, 20 Fairfield St., Boston.
J. G. Downing, Secretary, 520 Commonwealth Ave., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Mark Heiman, Chairman, 600 Medical Arts Bldg., Syracuse.
Timothy J. Riordan, Secretary, 136 E. 64th St., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA
SECTION ON DERMATOLOGY

William D. Whitehead, Chairman, Medical Arts Bldg., Scranton.
V. C. Garner, Secretary, Germantown Professional Bldg., Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Ruth Herrick, Chairman, 26 Sheldon Ave., S. E., Grand Rapids.
Eugene A. Hand, Secretary, 801 Second National Bank Bldg., Saginaw.

MINNESOTA DERMATOLOGICAL SOCIETY

E. M. Rusten, President, 78 S. 9th St., Minneapolis.
F. W. Lynch, Secretary-Treasurer, Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Onis George Hazel, President, Osler Bldg., Oklahoma City.
Everett S. Lain, Secretary, Medical Arts Bldg., Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

Everett R. Seale, President, 1215 Walker Ave., Houston.
Duncan O. Poth, Secretary, 414 Navarro St., San Antonio.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Francis A. Ellis, President, 104 W. Madison St., Baltimore.
I. Louis Sandler, Secretary, 1835 I St., N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Samuel M. Peck, President, 125 E. 72d St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

M. J. Cantor, President, 907 St. Marks Ave., Brooklyn.
S. H. Silvers, Secretary, 920 Bushwick Ave., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Richard L. Saunders, President, 333 Linwood Ave., Buffalo.
James W. Jordon, Secretary, 471 Delaware Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Harry D. Parkhurst, President, 264 Genesee St., Utica.
Maxwell C. Snider, Secretary, 106 Oak St., Binghamton.

CHICAGO DERMATOLOGICAL SOCIETY

Edward A. Oliver, President, 55 E. Washington St., Chicago.
Herbert Rattner, Secretary, 25 E. Washington St., Chicago.

CINCINNATI DERMATOLOGICAL SOCIETY

Adolph B. Loveman, President, 332 W. Broadway, Louisville, Ky.
Daniel J. Kindel, Secretary-Treasurer, Union Central Bldg., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except June, July, August and September.

Cleveland Dermatological Society

John Gammel, President, 1020 Huron Rd., Cleveland.
Charles G. La Rocco, Secretary, 2060 E. 9th St., Cleveland.

Detroit Dermatological Society

G. Warren Hyde, President, 2501 W. Grand Blvd., Detroit.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.
Place: Detroit. Time: May 1939.

Kansas City (Mo.) Dermatological Society

C. C. Dennie, President, 1103 Grand Ave., Kansas City.
Thomas B. Hall, Secretary, 902 Professional Bldg., Kansas City.

Los Angeles Dermatological Society

Thomas W. Nisbet, President, 65 N. Madison Ave., Pasadena, Calif.
C. R. Caskey, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

Max Scheer, Chairman, 509 Madison Ave., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.

Montreal Dermatological Society

L. P. Ereaux, President, 1390 Sherbrooke St., W., Montreal, Canada.
Paul Poirier, Secretary, 456 Sherbrooke St., E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Eugene F. Traub, Chairman, 140 E. 54th St., New York.
Louis Tulipan, Secretary, 224 E. 17th St., New York.

New York Dermatological Society

J. Frank Fraser, President, 100 W. 59th St., New York.
Frank C. Combes, Secretary, 80 W. 40th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln, Neb.

Philadelphia Dermatological Society

Thomas Butterworth, Chairman, 411 Walnut St., Reading, Pa.
Herman Beerman, Secretary, 255 S. 17th St., Philadelphia.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

John C. Kerr, President, 62–14th St., Wheeling, W. Va.
Marvin B. Goldstein, Secretary, Stambaugh Bldg., Youngstown, Ohio.
Time: Third Thursday of every month except July and August.

St. Louis Dermatological Society

Martin F. Engman Jr., President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

Merlin T.-R. Maynard, President, San Jose, Calif.
H. V. Allington, Secretary, 3115 Webster St., Oakland, Calif.
Time: Third Friday of February, April, September and November.